IPSO-NITRATION STUDIES

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ABSTRACT

In the first part of the thesis the reaction of 1,3,5-trichloro-2,4,6-trimethylbenzene (32) with fuming nitric acid is shown to give the C2-epimeric pair of 6-hydroxy-2,5-dinitrocyclohex-3-enones (42) and (43). Rearrangement of each of those hydroxydinitro compounds under mildly basic conditions gives mixtures of the C1-epimeric 2,5-dinitrocyclopent-3-en-1-ols. Similar acyloin rearrangement studies are reported for the hydroxydinitro compounds (8),(10),(29) and (30). During the course of these base-catalysed rearrangements an unusual rearrangement was observed of 1-acetyl-3,*t*-5-dichloro-2,4-dimethyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (50) in acetone to give the unexpected C6-epimeric compound, 3,*t*-5-dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (54).

Nitration of the polysubstituted 6-methylphenols, 2,3,4,5-tetrabromo-6-methylphenol (2), 2,4,5-tribromo-3,6-dimethylphenol (5), 3,4,5-tribromo-2,6-dimethylphenol (28), 3,5-dichloro-2,4,6-trimethylphenol (41) and 2,4-dibromo-3,5,6-trimethylphenol (57), with fuming nitric acid in acetic acid had been shown earlier to give 6-hydroxy-2,5-dinitrocyclohex-3-enones. In the second part of the thesis the corresponding reactions of these phenols with nitrogen dioxide in either cyclohexane or acetic acid are discussed. For most compounds the reaction products are identical with those obtained from the fuming nitric acid nitration, except that for 2,4-dibromo-3,5,6-trimethylphenol (57) 2,5,6-trinitrocyclohex-3-enones are obtained in the nitrogen dioxide reactions.

In the third part of the thesis the study of the reactions of phenols with nitrogen dioxide, in cyclohexane or benzene,

is extended to the 2,4,6-trialkylphenols, 4-t-butyl-2,6-dimethylphenol (66), 2-t-butyl-4,6-dimethylphenol (79), 2,4-di-t-butyl-6-methylphenol (84), 2,6-di-t-butyl-4-methylphenol (62) and 2,4,6-tri-t-butylphenol (98). These compounds give a diverse range of products arising from initial *ipso* substitution, but the structures of the products which are formed can be accommodated within a mechanistic scheme which is discussed.

In the final part of the thesis is described the formation of a phenol coupling product, 4-t-butyl-*r*-2-(4'-t-butyl-2',6'-dimethylphenoxy)-*t*-6-hydroxy-2,6-dimethyl-*t*-5-nitrocyclohex-3-enone (109), in a reaction mixture derived from the reaction of 4-t-butyl-2,6-dimethylphenol (66) with one molar-equivalent of nitrogen dioxide. The structure of this compound is determined.

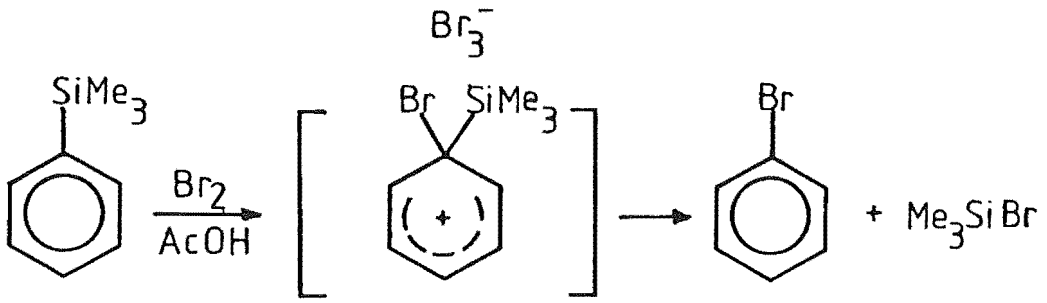
Throughout the thesis extensive use is made in product structure determination of single crystal X-ray analysis and, in all, seventeen crystal structures are reported.

CHAPTER 1

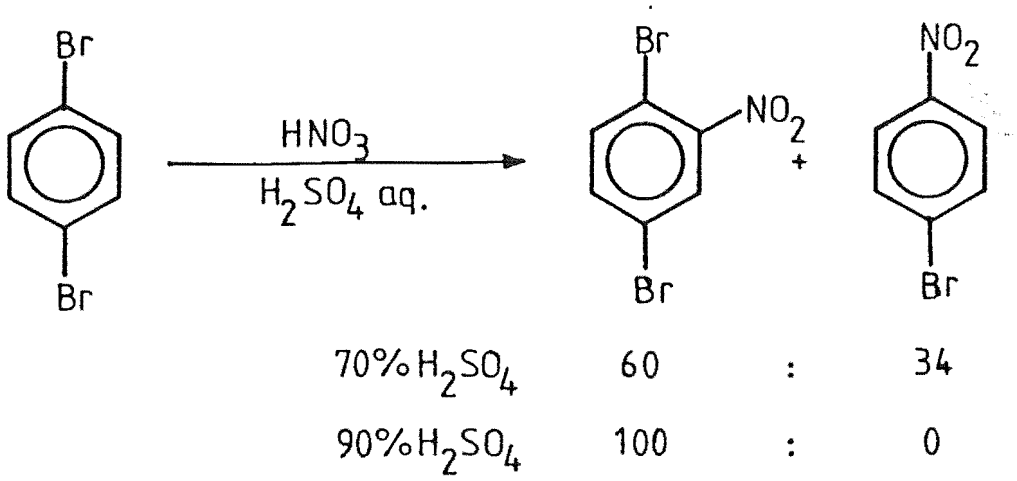
GENERAL INTRODUCTION

1.1 BACKGROUND

The prefix "*ipso*" was introduced by Perrin and Skinner[1] to denote attack by a reagent at a substituted position on a benzene ring. This phenomenon had long been known for one of its consequences (*ipso*-substitution) in many electrophilic substitution reactions.[2] For example, the bromination of trimethylsilylbenzene gives bromobenzene and trimethylsilylbromide by an *ipso* substitution process:[2b]

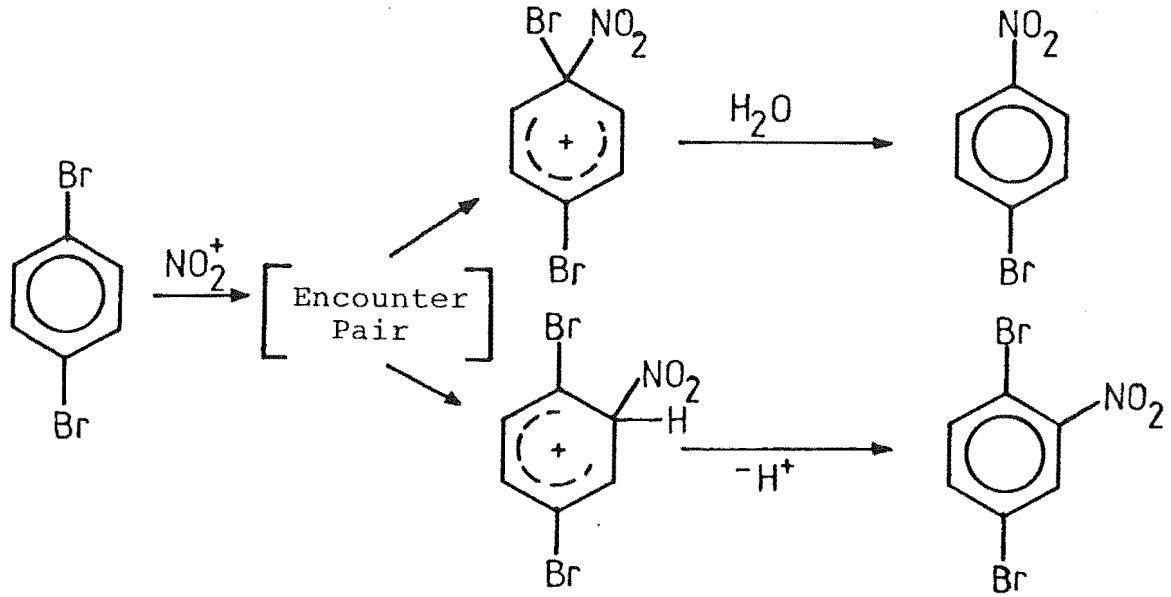


In nitration especially, *ipso* substitution and other results of *ipso* attack (notably, side-chain modification) had often been observed and regarded as "non-conventional".[3] For example, nitration of 1,4-dibromobenzene in sulphuric acid gives both 2,5-dibromonitrobenzene and 4-bromonitrobenzene but the product ratio is dependent on the sulphuric acid concentration:[3]



70% H_2SO_4	60	:	34
90% H_2SO_4	100	:	0

It is only recently that these effects have been shown to be consequences of *ipso* attack.[3,4] For example, in the nitration above, formation of 4-bromonitrobenzene results from the debromination of the intermediate w_i^{Br}.

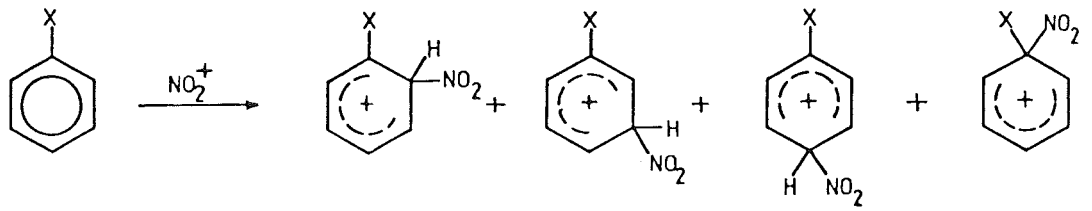


1.2 *ipso* ATTACK AND ITS CONSEQUENCES

1.2.1 WHELAND INTERMEDIATES FROM *ipso* ATTACK

In the electrophilic nitration of a monosubstituted benzene, the Wheland intermediates (w_s) formed are of two

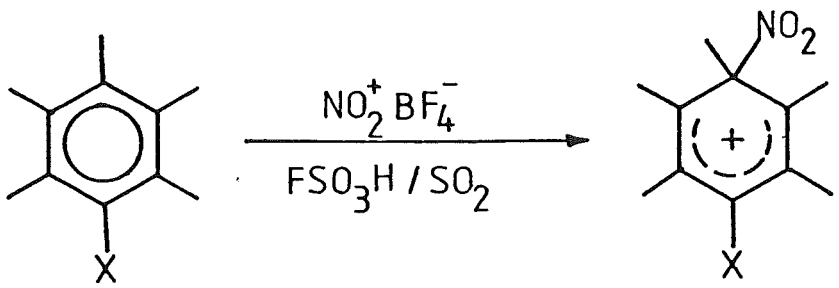
distinct kinds, those in which the nitro group is attached to an unsubstituted position (W_o, W_m, W_p) and that in which it is attached to the same position as the substituent (W_i^X), that is:



W_o W_m W_p W_i^X

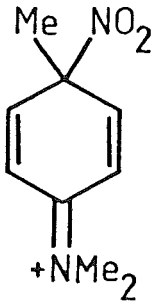
Direct observations of the first kind of Wheland intermediate are rarely reported and, generally, their chemistry is limited to proton loss.

In contrast, the observation and capture of W_i^X has been achieved in special cases. For example, some hexasubstituted benzenes give the cations in the absence of bases or nucleophiles.[5]



Particularly stable W_i^X's can be generated when a stabilising group is present at the *para* position (with respect to the *ipso* position). For example, in the nitration of

N,N-dimethyl-*p*-toluidine in 70% sulphuric acid at 0°, 4-methyl-2-nitro-N,N-dimethylaniline is produced *via* the stablised w_i^{Me} cation:[6]

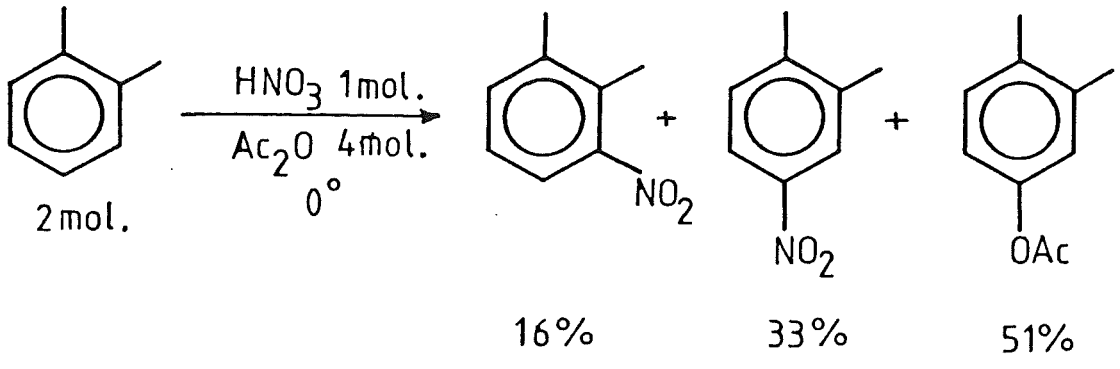


1.2.2 FATE OF w_i^X

a) REACTION WITH NUCLEOPHILES

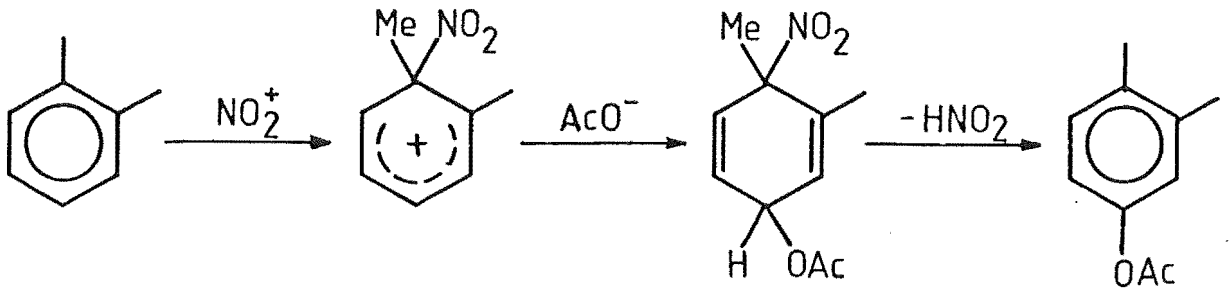
The capture of w_i^X by nucleophiles was one of the reactions which first drew attention to *ipso* attack in nitration and hence it warrants some mention.

For example, aryl acetates are found among the products of nitration of methylbenzenes with solutions prepared from nitric acid and acetic anhydride.[7]



The ratio of nitration to acetoxylation was found to be dependent on the substrate nature but not on its concentration.

The mechanism of acetoxylation was suggested to involve capture of the W_i^{Me} intermediate by acetate followed by elimination of nitrous acid to give the aryl acetate product.

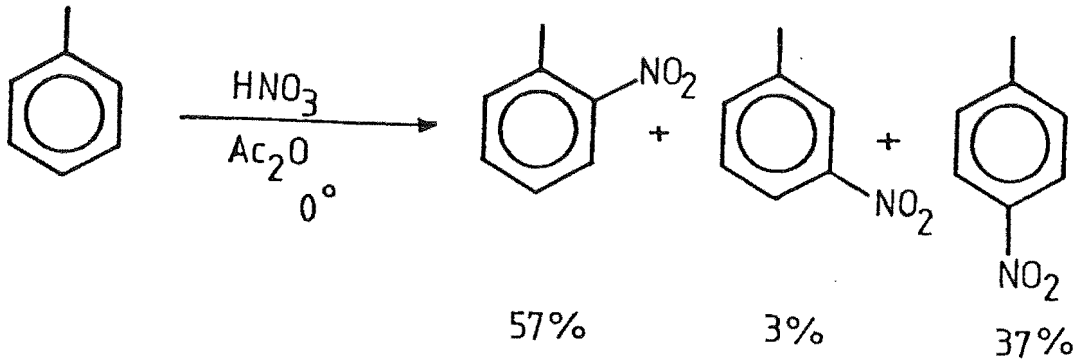


This mechanism was confirmed by the isolation of the stereoisomeric adducts,

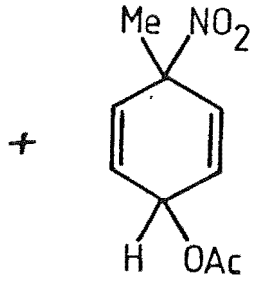
formed during the nitration of *o*-xylene.[8] Similar products were obtained from other aromatic substrates, mainly by Fischer and co-workers.[9]

Usually, nitro-acetate formation is accompanied by the products of conventional nitration and the division of the starting material among these different kinds of products gives important information about positional reactivities in the

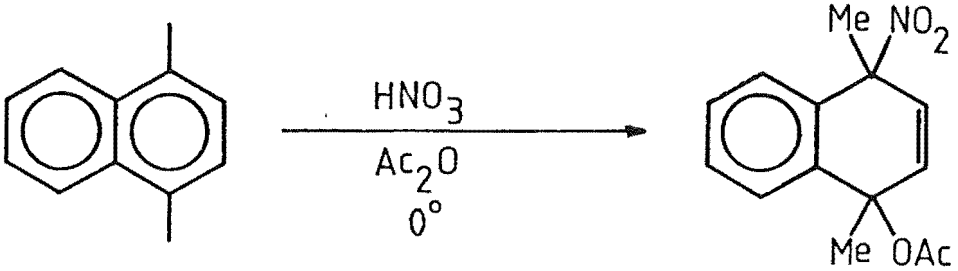
aromatic substrate.[10] The yields of adduct vary markedly, accounting for only a few percent of the aromatic, as in the case of toluene, or for almost all of it, as with 1,4-dimethylnaphthalene.[11]



57% 3% 37%

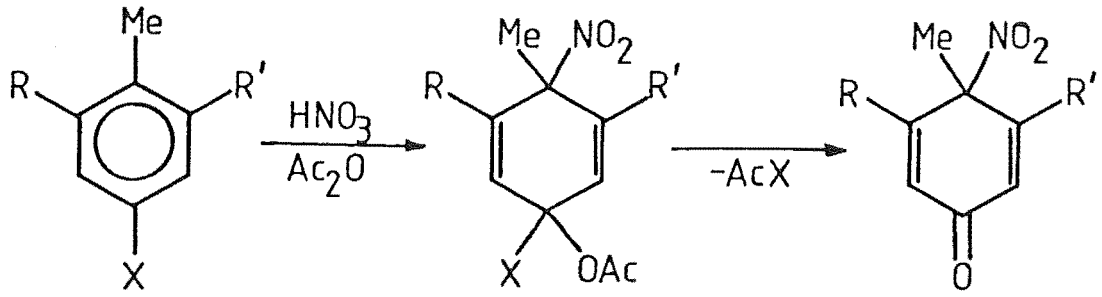


3%



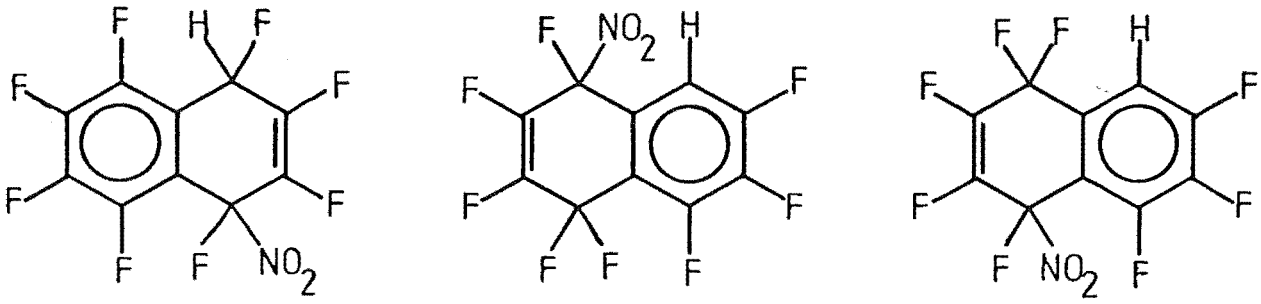
100%

In some cases the nitro-acetate adducts react further to give dienones, for example,



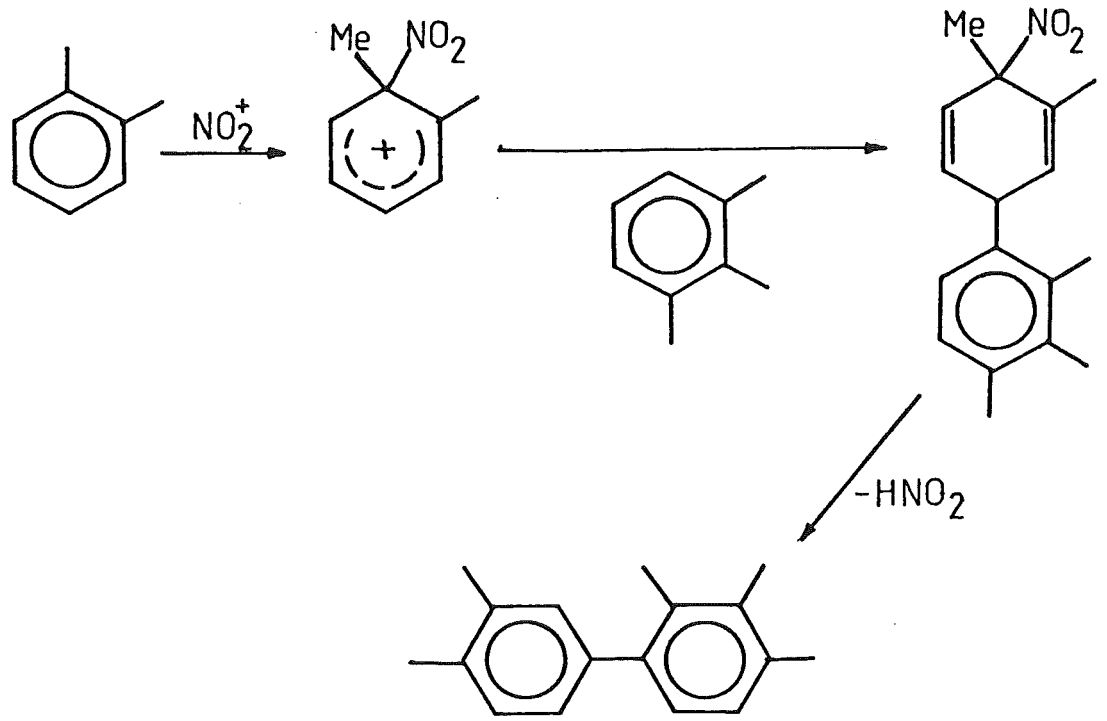
the yield of dienone being dependent on the nature of the substituents X, R and R'.[12]

Nitration of fluorinated aromatics with nitric acid in hydrofluoric acid gives dienes by *ipso* nitration followed by capture of the Wheland intermediate by fluoride ion. Thus, 1H-heptafluoronaphthalene gives the following adducts,[13a]



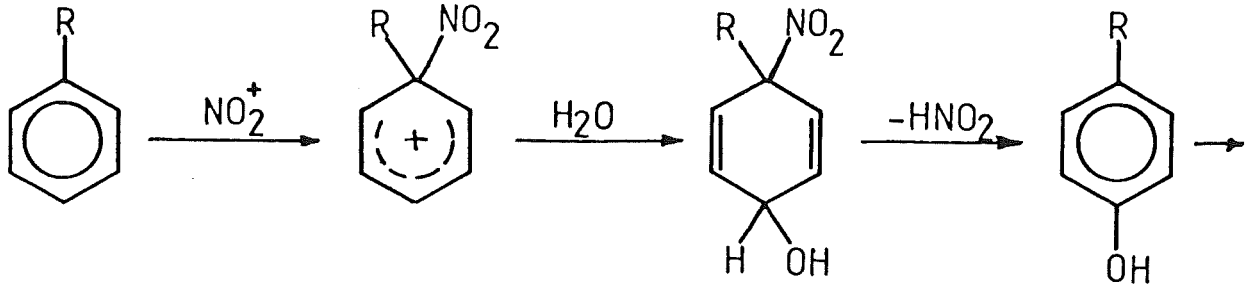
Similar reactions occur with pentafluorotoluene, chloro- and bromo-pentafluorobenzene and hexafluorobenzene.[13]

Some aromatic compounds (notably 1,2-dialkylbenzenes, hemimellitene and prehnitene) give biphenyls as well as nitration products when nitrated with nitric acid.[14]

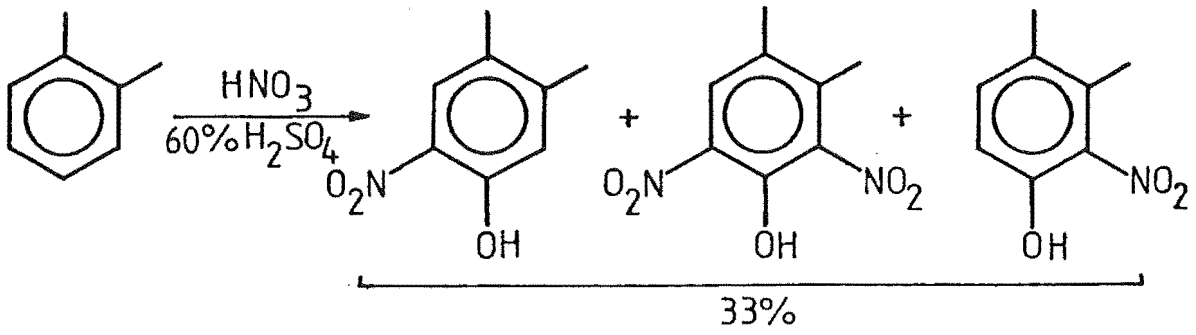


By analogy with the reactions of the nitrocyclohexadienyl acetates, the mechanism proposed above involves the w_i^x intermediate and indeed, biphenyls can be generated by reacting the nitrocyclohexadienyl acetates with aromatic substrates in trifluoroacetic acid.[15]

w_i^x's can react with water to give adducts which rearrange readily to phenols by loss of nitrous acid.



When nitration of aromatic substrates is carried out in aqueous acids, a significant proportion of the W_i^X may be captured by water resulting in a decreased yield of nitro aromatic product and a significant formation of nitrophenols.[16,17,18] For example, the nitration of *o*-xylene by nitric acid in 60% sulphuric acid gives a 33% yield of mono- and dinitro-3,4-dimethylphenols.[17]



+ nitro-xylenes.

b) MIGRATION OF THE NITRO GROUP

Wheland intermediates and dienones formed in electrophilic *ipso* nitration appear to be capable of rearrangement by migration of the nitro group or, less commonly, migration of the substituent X.

Three modes of nitro migration need to be considered, due to their differing consequences. These may be characterised as (i) intramolecular, (ii) extramolecular and (iii) intermolecular migration.[19]

Intramolecular migration is characterised in that the nitro group never becomes sufficiently free from the carbon structure to do other than move to a position adjacent to the *ipso* position (a 1,2-migration).

In extramolecular migration the nitro group becomes free enough to be able to *distinguish* and select amongst the positions in the carbon structure, but it does not leave the "encounter-pair" containing the carbon structure and itself.

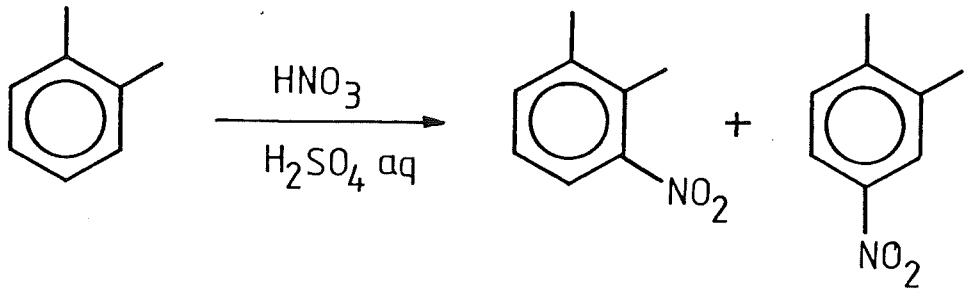
In intermolecular migration the *ipso* nitro group leaves its position, diffuses into the solvent and may react with carbon structures other than the one it left.

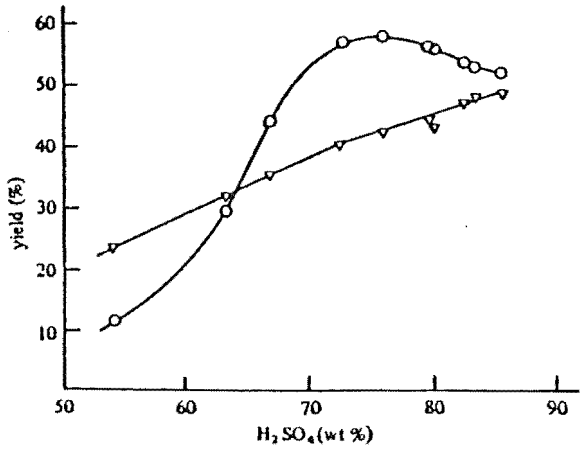
Extramolecular migration occurs when the nitration producing W_i^x proceeds at the encounter rate and intermolecular migration when it is slower than the encounter rate.

The importance of nitro migration (especially intra- and extra-molecular migration) in this present work, as will be demonstrated later, justifies a more complete examination of these migration processes.

INTRAMOLECULAR MIGRATION

Intramolecular 1,2-migration was first suggested by Myhre[17] as an explanation for the acidity dependence of the ratio of 3- to 4-nitro-*o*-xylene produced in the nitration of *o*-xylene in sulphuric acid.[20]





Nitration of *o*-xylene. Yields of 3-nitro (circles) and 4-nitro-*o*-xylene (triangles) as percentages of the starting material.

The proposed mechanism is illustrated in Scheme 1*. He suggested that the W_i^{Me} was captured by water at low acidities but that with increasing acidity 1,2-migration became important. Solvolysis of the nitro-acetate adduct of the W_i^{Me} (Scheme 1) gave only 3-nitro-*o*-xylene and 3,4-dimethylphenol, demonstrating that return of the W_i^{Me} to the encounter pair (the step necessary to produce 4-nitro-*o*-xylene) does not, in this case, compete with nitro migration to produce 3-nitro-*o*-xylene or capture by water to produce 3,4-dimethylphenol.

EXTRAMOLECULAR MIGRATION

Extramolecular 1,3-migration of nitro was first invoked to explain the presence of nitrophenols in the reaction products of the electrophilic nitration of anisole derivatives.[21,22] For example, 4-methylanisole nitrates in sulphuric acid to give 4-methyl-2-nitrophenol as well as 4-methyl-2-nitroanisole.[21]

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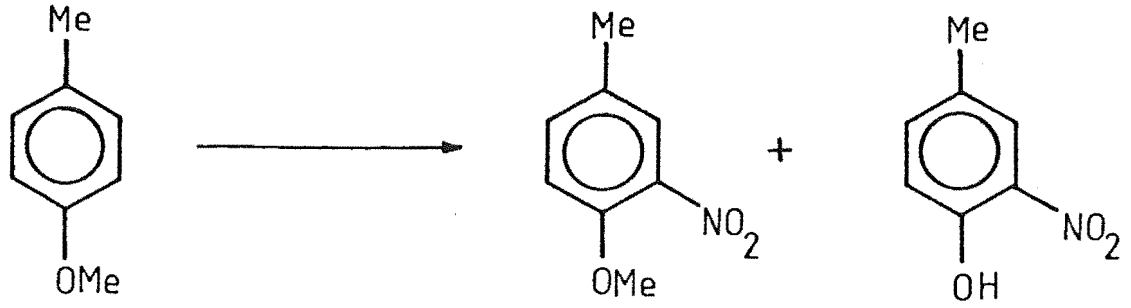
* Schemes 1-6 as foldouts at the end of General Introduction

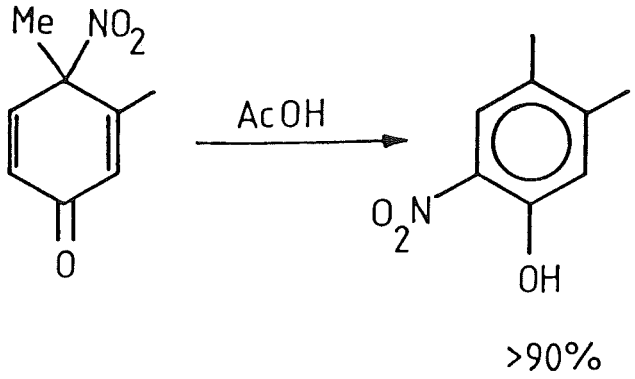


40% H_2SO_4	6	:	4
83% H_2SO_4	8	:	2

The proposed mechanism is illustrated in Scheme 2. A nitrocyclohexa-2,5-dienone (1), identical to a species formed by nitration of *p*-cresol, is formed and decays during the reaction.[23] In strong acid the conjugate acid of the dienone (1) rearranges to give the 2-nitrophenol *via* dissociation to an encounter pair which rapidly recombines. This is consistent with the kinetic evidence that *p*-cresol and *p*-methylanisole are nitrated at the encounter rate so that the components of the two encounter pairs do not diffuse back into the medium. In contrast, *p*-chloroanisole nitrates at a rate well below the encounter limit and gives 4-chloro-2-nitrophenol and 4-chloro-2-nitroanisole[1,24] or 4-chloro-2,6-dinitrophenol only,[25] depending on concentration effects. In accordance with the proposed mechanism 4-chlorophenol was detected in the reaction, it having "leaked" from the encounter pair. Studies using $H_2{}^{18}O$ enriched reaction mixtures have confirmed these suggestions.[26]

Of particular importance to this present work was the extramolecular migration involved in the rearrangement of 4-nitrocyclohexa-2,5-dienones. These compounds rearrange, when the *ortho*- positions are not substituted, to give *o*-nitrophenols.[12] For example, the 4-nitrocyclohexa-2,5-dienone

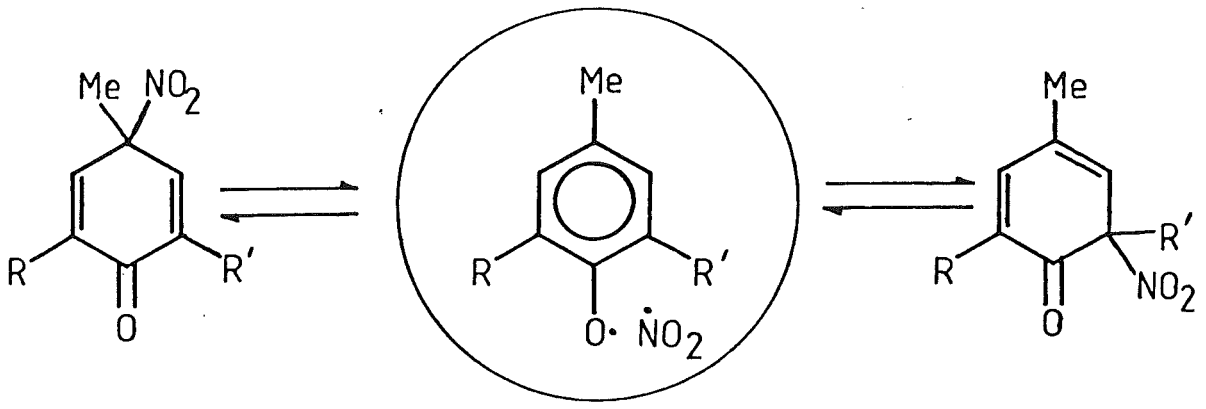
derived from *o*-xylene decomposes almost quantitatively to 4,5-dimethyl-2-nitrophenol,[12b]



>90%

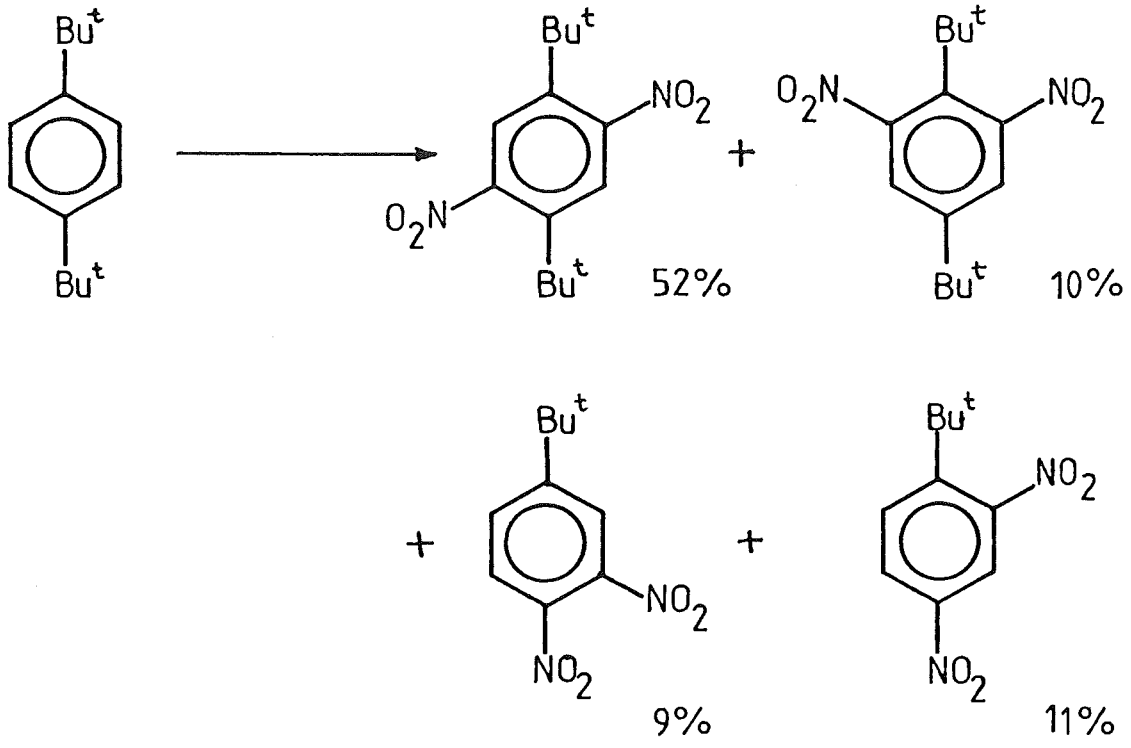
The conversion of 4-methyl-, 3,4-dimethyl- and 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dienones to the corresponding *o*-nitrophenols in hexane, acetic acid, ethanol, water and dimethyl sulphoxide has been shown to proceed by the radical dissociation-recombination mechanism shown in Scheme 3.[12c]

An important assumption in this present work is that the radical dissociation-recombination mechanism shown in Scheme 3 operates even when the *ortho*- positions <u>are</u> substituted. In such cases the pathway for the formation of the *o*-nitrophenols is removed and an equilibrium is established between the 4-nitro and 6-nitrocyclohexadienones.

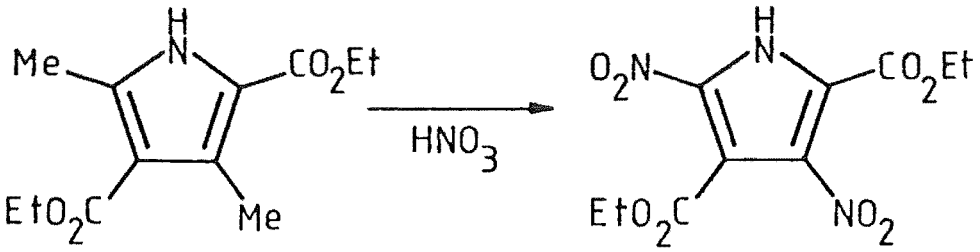


1.2.3 *ipso* - SUBSTITUTION

ipso-substitution is the longest-known consequence of *ipso* attack and was the main contributor to the description "anomalous nitration".[3a] It occurs when the *ipso* group (other than the nitro) is acyl, alkyl, arylazo, aryloxy, carboxyl, halogen, methoxyl, phosphonyl, silyl or sulphonyl. This area is apparently well-documented,[27] but in some cases the mode of removal of the non-nitro *ipso* group is a matter for debate. For instance, in the nitration of 1,4-di-t-butylbenzene approximately 20% of the substrate undergoes nitrode-t-butylation,[28]



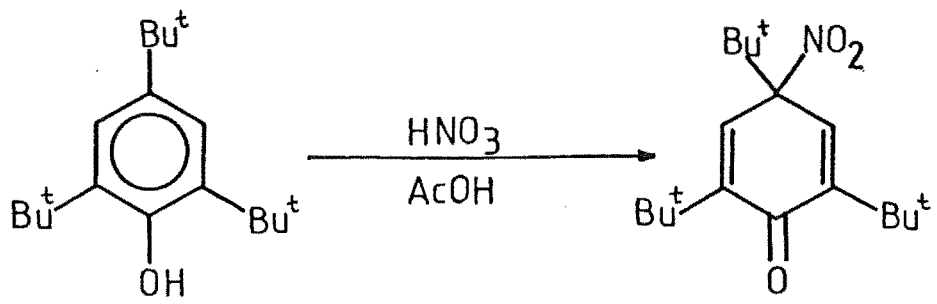
This process involves loss of the stable t-butyl cation from the *ipso* Wheland intermediate as the essential step. In contrast, the nitration of diethyl 2,4-dimethylpyrrole-3,5-dicarboxylate gives diethyl 2,4-dinitropyrrole-3,5-dicarboxylate,[29]



It is unlikely that the reaction involves loss of the highly unstable methyl cation; preliminary modification (most likely oxidation) of the methyl group probably occurs prior to its loss.

Alkyl group modification is a very large field of study in *ipso* substitution[30] and to attempt to summarise it here would be impractical considering that the main body of work presented in this present work does not involve alkyl group modification.

A major consequence of some ipso substitution reactions is the modification of a substituent. The earliest such reports[31] concern the transformation of a phenolic hydroxyl group into a ketone function. Most substituted 4-methylphenols form 4-nitrodienones[3d,32] and in some cases, especially with 2,4,6-trisubstituted phenols,[33] the 4-nitrodienones are relatively stable. For example, nitration of 2,4,6-tri-t-butyl-phenol gives the corresponding 4-nitrocyclohexa-2,5-dienone,[33]



These 4-nitrodienones are relatively stable and decompose slowly to give *p*-quinones. The mechanistic details of this transformation are limited.[3d]

1.3 NITRATION OF POLYSUBSTITUTED PHENOLS WITH FUMING NITRIC ACID

In 1907 Zincke and Klostermann reported[34] the nitration of 2,3,4,5-tetrabromo-6-methylphenol (2) (Refer Block A)* with fuming nitric acid in acetic acid to give a cyclohexadiene derivative (3). Trituration of this compound (3) with aqueous sodium carbonate solution or addition of water to the nitrating mixture of the phenol (2) was further reported[34] to give the acyclic derivative (4). Later, Zincke and Breitwieser reported[35] obtaining, from the nitration of 2,4,5-tribromo-3,6-dimethylphenol (5) with fuming nitric acid, the analogous products (6) and (7). Similar results were obtained[36] by Zincke and Preiss for chlorinated 6-methylphenols.

It was shown[37] recently by X-ray crystal structure analysis that the compounds reported by Zincke *et. al.* as (6) and (7) have the structures (8) and (9) respectively (and by analogy (3) and (4) have the structures (10) and (11)) (Refer Block A).

The notable features of structure (8) are the all *cis*-arrangement of the hydroxy and nitro functional groups at C2, C5 and C6 and the introduction of a nitro function at C5, *meta*- to the phenolic hydroxyl group.

A reaction scheme for the formation of the cyclohex-3-enones (8) and (10) is presented in Scheme 4. In this scheme,

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* Block A as foldout at end of General Introduction.

initial nitration of the phenol (2) proceeds to give 4-nitrocyclohexa-2,5-dienone (12) and/or 6-nitrocyclohexa-2,4-dienone (14). An equilibrium is established between the 4-nitrodienone (12) and the 6-nitrodienone (14) in solution and the 6-nitrodienone (14) undergoes a nitro-nitrito rearrangement to give the 6-nitritocyclohexa-2,4-dienone (16). Hydrolysis of the 6-nitritodienone (16) in solution gives the 6-hydroxycyclohexa-2,4-dienone (18) which will exist in conformation (18a) due to strong intramolecular carbonyl-hydroxyl hydrogen bonding. In this conformation the C6-methyl group is held in such a position that it effectively shields the lower face of the diene system. Concerted addition of dinitrogen tetroxide could then occur to the upper face of the diene system to give the observed all-*cis* stereochemistry of the C6-hydroxyl, C2-nitro and C5-nitro functions in cyclohex-3-enone (10). A similar process applies for phenol (5) (Refer Scheme 4).

Extensive study[38] of the nitration of phenols (2) and (5) in acetic acid has provided evidence supporting the reaction sequence in Scheme 4. For example, nitration of the polysubstituted phenols (2) and (5) with stoichiometric quantities of nitric acid in acetic acid gave the 4-nitrocyclohexa-2,5-dienones (12) and (13) respectively, and it was shown[38] by ^{1}H n.m.r. and ultraviolet absorption spectroscopy that an equilibrium existed between the 4-nitrodienones (12) and (13) and their respective 6-nitro-cyclohexa-2,4-dienones (14) and (15) in solution.

Conversion of the 4-nitrodienones (12) and (13) into the corresponding 6-hydroxycyclohexa-2,4-dienones (18) and (19) (presumably *via* the 6-nitrodienones (14) and (15) and the 6-nitritodienones (16) and (17)) could be achieved in acetic

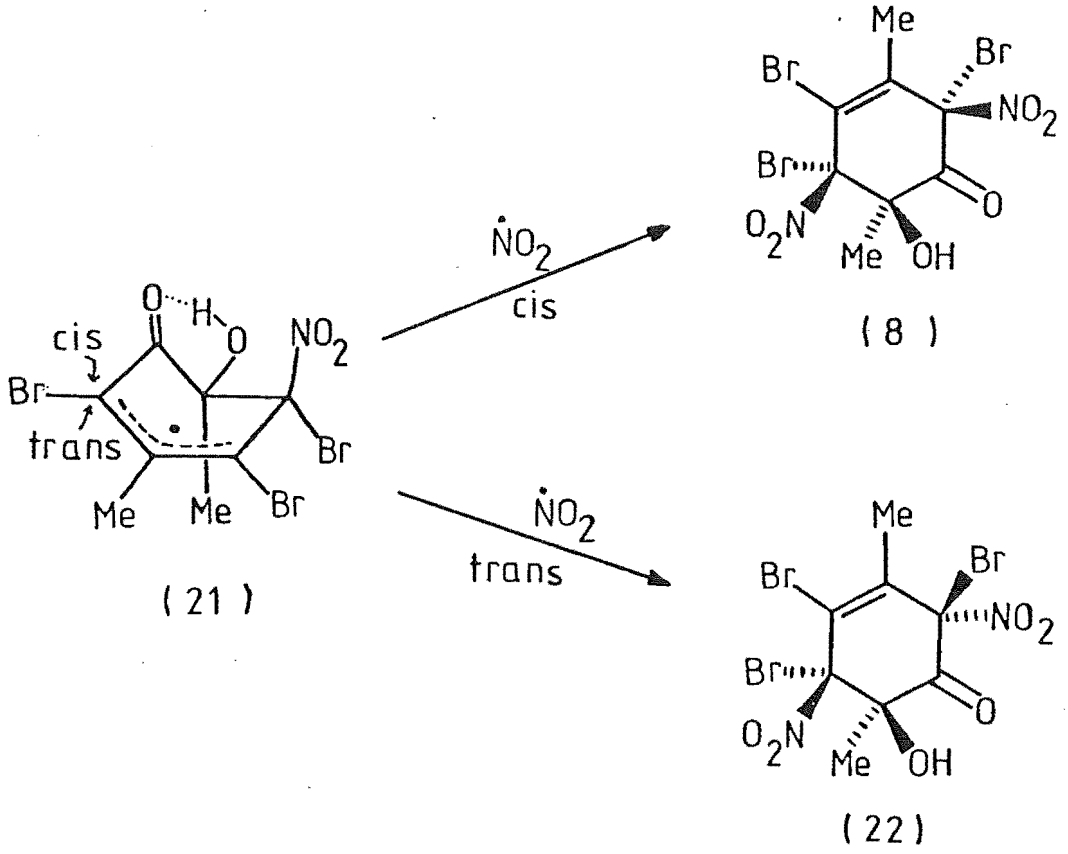
acid solution and it was shown that addition of dinitrogen tetroxide (N_2O_4) to these 6-hydroxydienones (18) and (19) gave the hydroxydinitrocyclohex-3-enones (10) and (8) respectively.

That this latter step is reversible was demonstrated[38] by heating either of the hydroxydinitrocyclohex-3-enones (10) or (8) in chloroform for a short period to yield, by extrusion of dinitrogen tetroxide, the 6-hydroxydienones (18) or (19) respectively.

In contrast, a chloroform solution of the hydroxydinitrocyclohex-3-enone (8) left standing at room temperature for 48h afforded the α-diketone (20)[38] (Refer Scheme 5). This difference in behaviour for compound (8) in chloroform at different temperatures can be explained by the radical dissociation-recombination mechanism shown in Scheme 5. Reversible, homolytic C2-NO_2 bond cleavage in the hydroxydinitroketone (8) gives a pair of radicals enclosed in a solvent cage. At 20°, within the solvent cage, C2-ONO bond formation can occur followed by loss of the constituents of NOBr to give the α-diketone (20). At the boiling point of chloroform, diffusion of the radical pair from the solvent cage occurs more readily to give nitrogen dioxide radical plus the separated carbon radical (21), which would yield the 6-hydroxydienone (19) by further nitrogen dioxide loss. This stepwise loss of two nitrogen dioxide radicals from the hydroxydinitroketone (8) is in clear contrast to the proposed concerted addition of dinitrogen tetroxide to hydroxydienone (19) in Scheme 4.

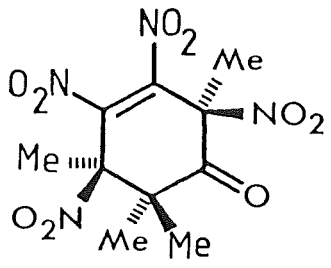
A stepwise addition of nitrogen dioxide radical to the 6-hydroxydienone (19) would be expected to give the intermediate radical (21) whose conformation would be similar

to (21a) (Refer Scheme 5). Subsequent attack of this radical (21) at carbon-2 by another nitrogen dioxide radical should be equally likely from either side of the ring, giving rise to both *cis*- and *trans*-2,5-dinitro stereochemistry in the cyclohex-3-enone products.

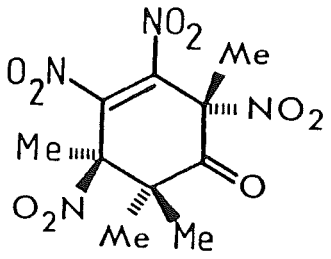


This is in clear contrast to the experimental isolation of only the *cis*-2,5-dinitrocyclohex-3-enone (8). A species corresponding to the *trans*-2,5-dinitrocyclohex-3-enone (22) was at no time observed or isolated.

During studies of the nitration of 1,2,3,4-tetramethyl-5,6-dinitrobenzene with fuming nitric acid in dichloromethane,[39] the two isomeric tetranitrocyclohex-3-enones (23) and (24) were isolated.

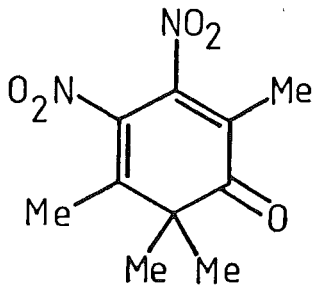


(23)



(24)

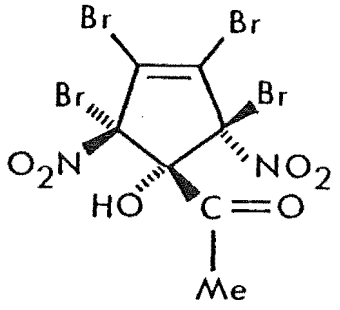
Heating either of the compounds (23) or (24) in carbon tetrachloride gave the dinitrodienone (25),[39]



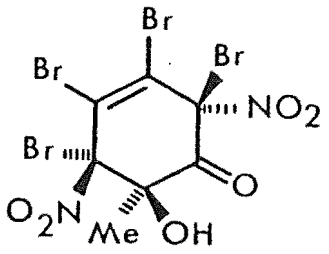
(25)

which when reacted with nitrogen dioxide in cyclohexane gave both of the tetranitroketones (23) and (24). Given the *trans*-2,5-dinitro stereochemistry of the compound (24), it seems unlikely that the addition of dinitrogen tetroxide to cyclohexa-2,4-dienone systems is a concerted process.

Indirect evidence for a *trans*-2,5-dinitroketone was reported[38] in the form of a long-term nitration product from 2,3,4,5-tetrabromo-6-methylphenol (2) which was isomeric with, but not identical to the dinitroketone (10) or its acyloin rearrangement product (11). It was assigned the structure (26) because of its spectroscopic similarity to compound (11) except that the absence of a symmetry plane was indicated in the ^{13}C n.m.r. spectrum.



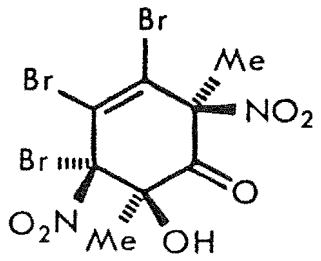
(26)



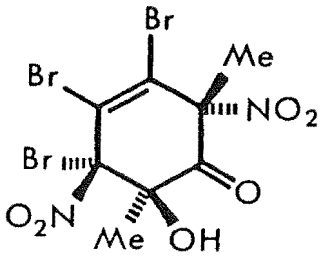
(27)

A cyclopentenol derivative such as (26) could only arise from the acyloin rearrangement of the corresponding *trans*-2,5-dinitrocyclohex-3-enone (27), a species never observed or isolated in the nitration of phenol (2).

The first clear example of hydroxydinitrocyclohex-3-enones with *cis*- and *trans*-2,5-dinitro stereochemistry came from the nitration of 3,4,5-tribromo-2,6-dimethylphenol (28) with fuming nitric acid in acetic acid[40] which yields the two C2-epimeric hydroxydinitroketones (29) and (30).

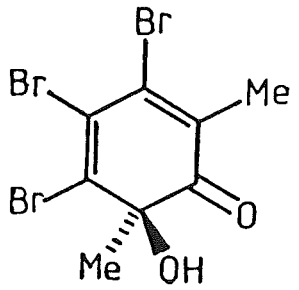


(29)



(30)

Heating either of the hydroxydinitroketones (29) or (30) in chloroform gave, by extrusion of dinitrogen tetroxide, the 6-hydroxydienone (31).



(31)

This compound (31), when reacted with nitrogen dioxide in cyclohexane, gave both of the hydroxydinitroketones (29) and (30).

A revised mechanism for the formation of the 6-hydroxy-2,5-dinitrocyclohex-3-enones, based on the observations outlined above, is outlined in Scheme 6. The stepwise conversion of the phenol (A) into the 4-nitrodienone (B), through the 6-nitrodienone (C) and 6-nitritodienone (D) to the 6-hydroxydienone (E) is essentially identical to Scheme 4. The main difference lies in the penultimate step involving addition of dinitrogen tetroxide, or its equivalent constituents, to the 6-hydroxydienone (E).

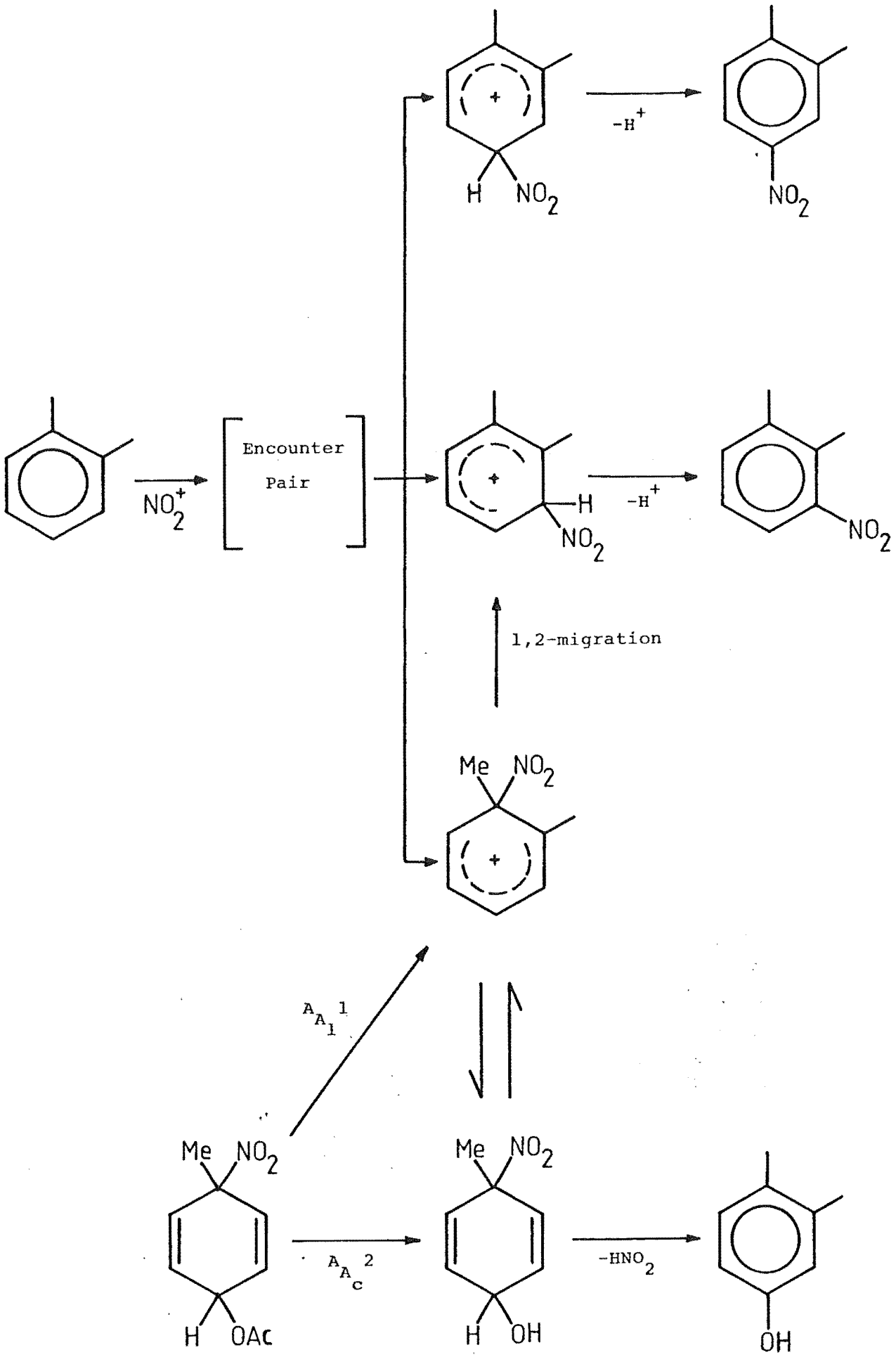
As in Scheme 4, the 6-hydroxydienone (E) has a conformation, determined by intramolecular carbonyl-hydroxyl hydrogen bonding, in which one face of the diene system is shielded by the C6-methyl group. Attack of the diene system at carbon-5 by nitrogen dioxide radical, the initiating step in the formation of the hydroxydinitrocyclohex-3-enones, can thus occur only from the direction *cis*- to the C6-hydroxyl group. The delocalised radical intermediate (F) thus formed is open to attack at carbon-2 by another nitrogen dioxide radical (although the direction of attack is now

much less specific because of the absence of steric hindrance by the C6-methyl group), the result being the formation of both *cis*- and *trans*-2,5-dinitro stereoisomeric products.

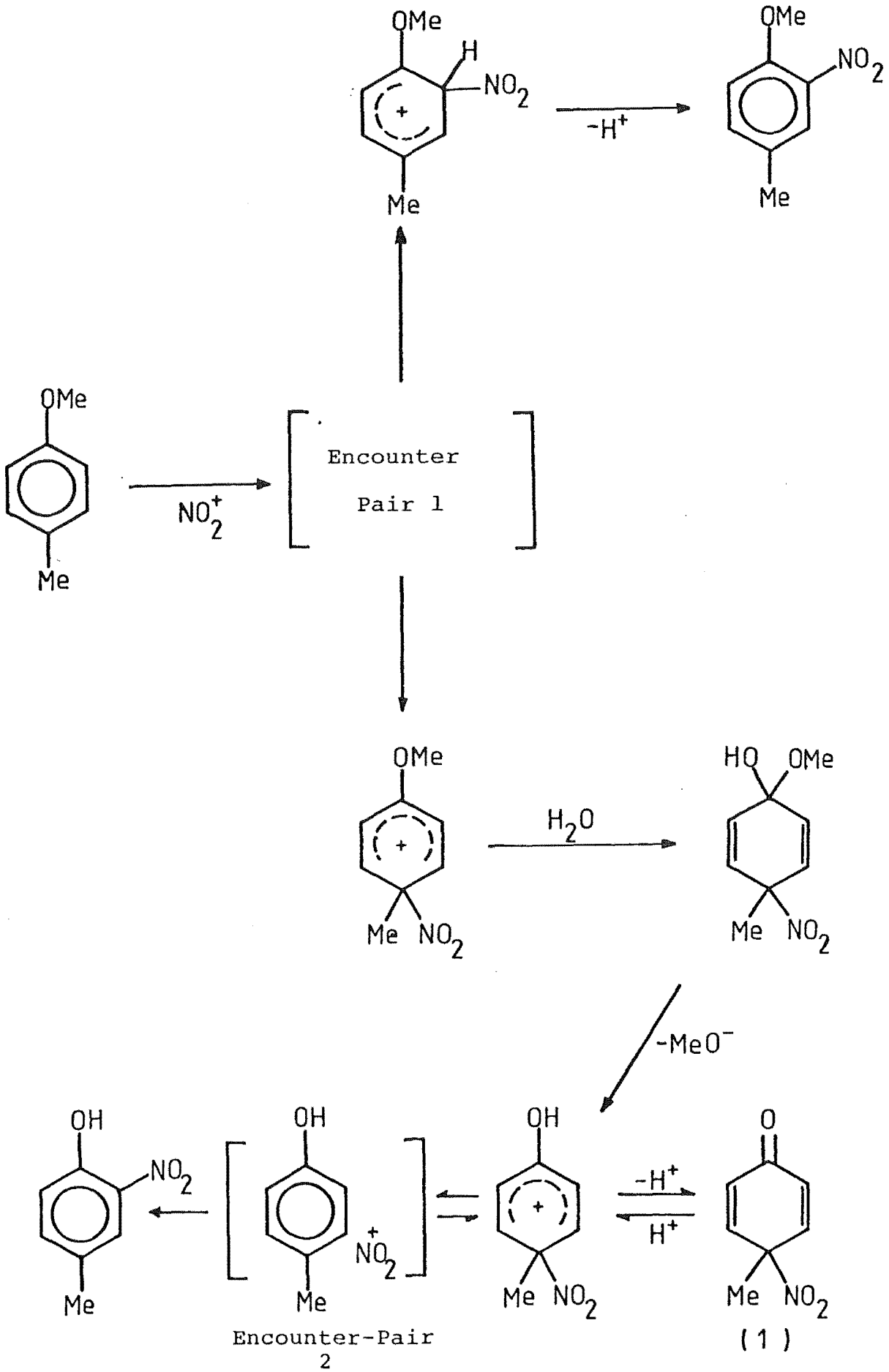
The need to investigate the validity and/or generality of this mechanism, or possible alternatives, was the primary reason that my Ph.D. research was undertaken. My work consisted of <u>two</u> principal sections:

The first section is concerned with the nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene with fuming nitric acid in dichloromethane. This reaction was originally reported by Suzuki *et.al.*[41]. Results from this section led subsequently to an extensive study of the base-catalysed acyloin rearrangements of 6-hydroxy-2,5-dinitrocyclohex-3-enones.

The second section is concerned with the nitration of polysubstituted phenols with nitrogen dioxide in non-polar, aprotic solvents and the comparison of these reactions with nitrations performed using fuming nitric acid.


Encounter
Pair
NO_2^+
$-H^+$
1,2-migration
Me
NO_2
H
OAc
OH
$A_{A_1}1$
$A_{A_c}2$
$-HNO_2$

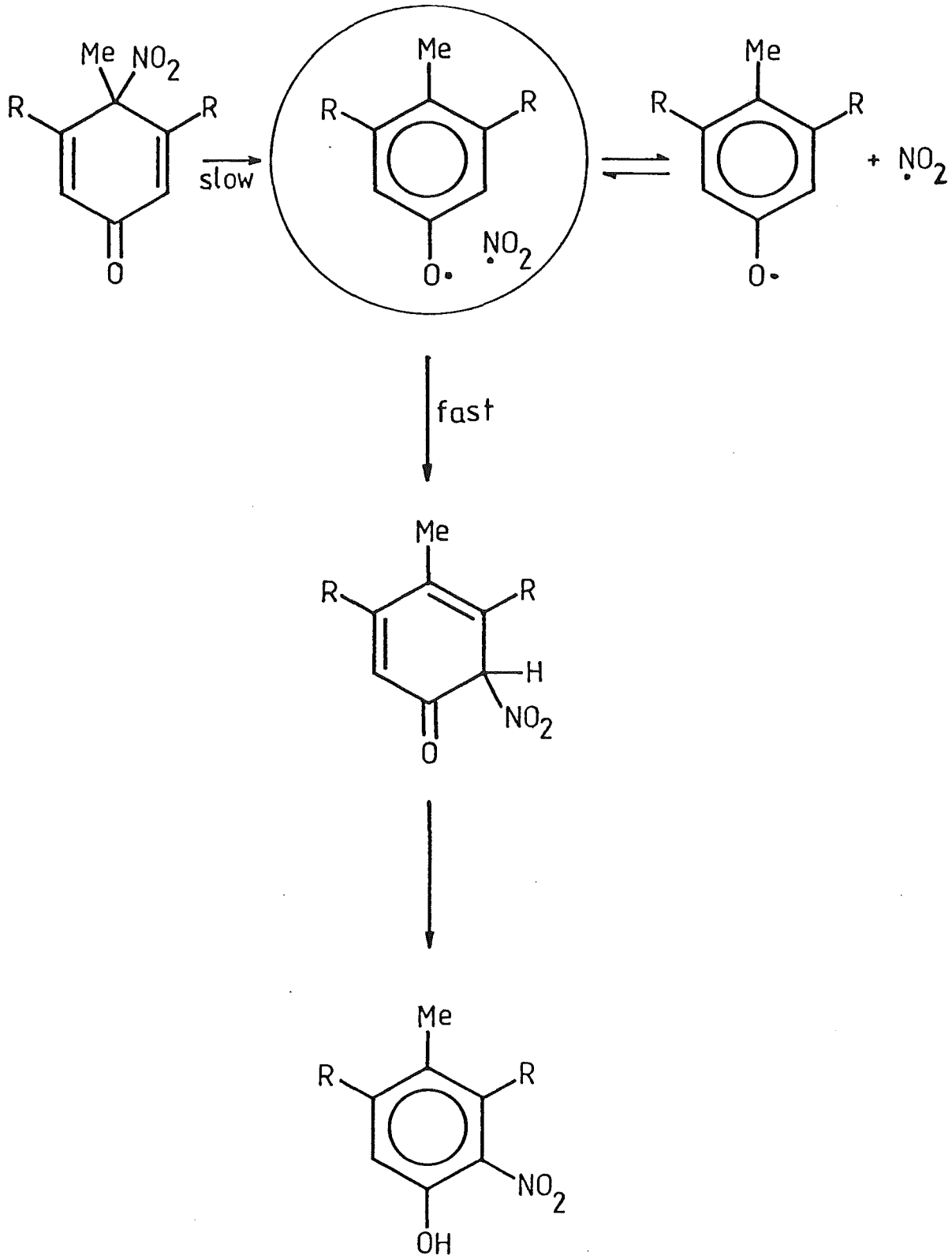
SCHEME 1.



Encounter-Pair 2

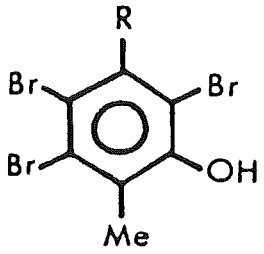
(1)

SCHEME 2.

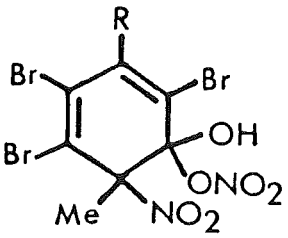

Me
NO2
R
R
O
slow
Me
R
R
O·
NO2
Me
R
R
O·
+ NO2
fast
Me
R
R
H
NO2
O
Me
R
R
NO2
OH

SCHEME 3.

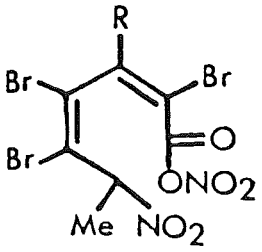
BLOCK A.



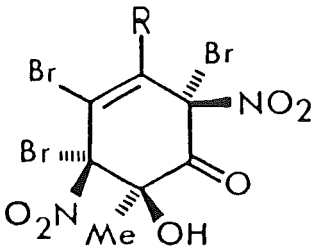
(2) R=Br
(5) R=Me



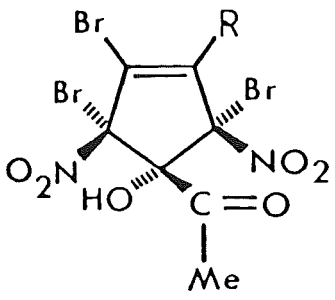
(3) R=Br
(6) R=Me



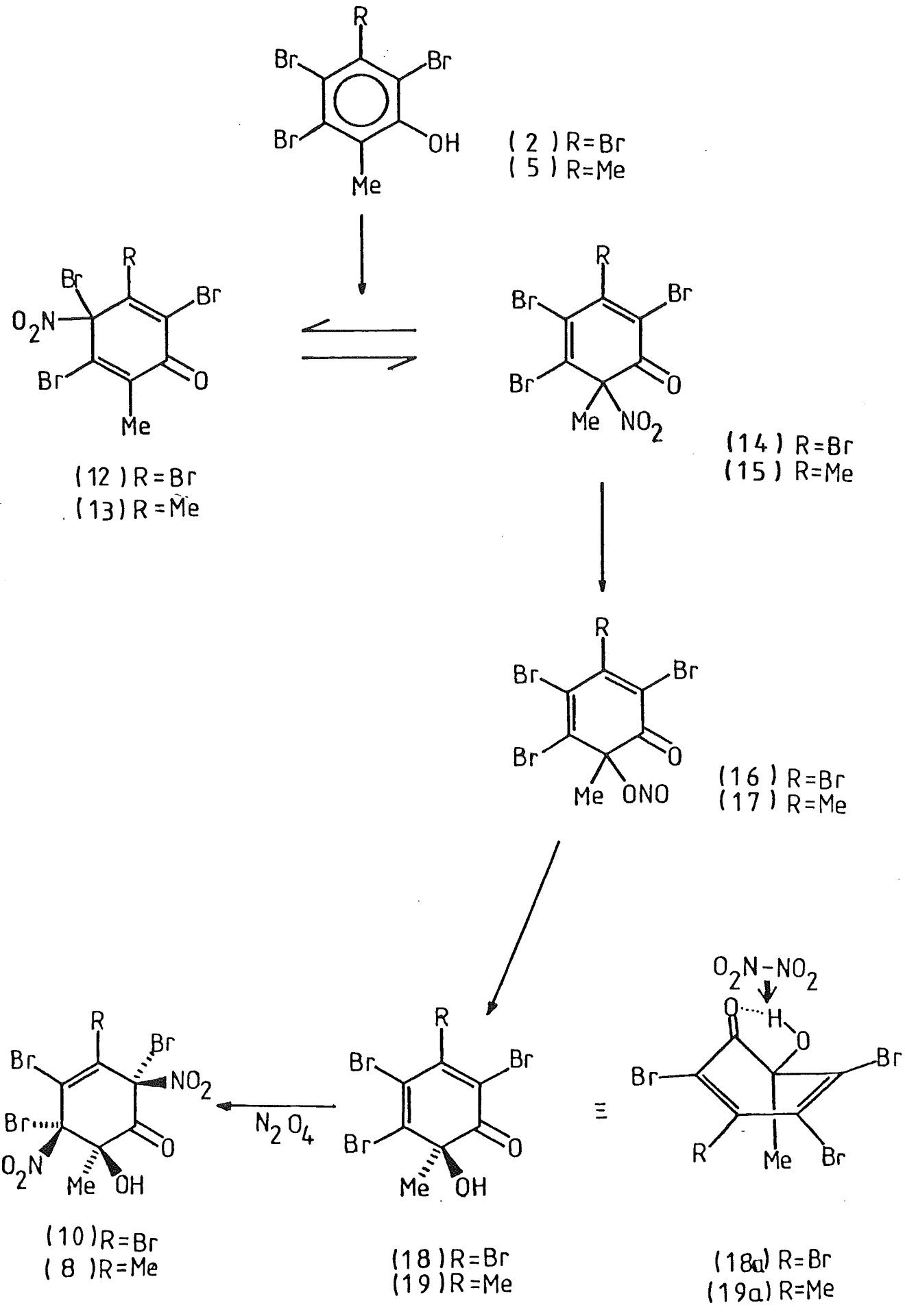
(4) R=Br
(7) R=Me



(10) R=Br
(8) R=Me



(11) R=Br
(9) R=Me


R
Br
Br
Br
OH
Me
(2) R=Br
(5) R=Me
R
Br
O_2N
Br
Br
O
Me
(12) R=Br
(13) R=Me
R
Br
Br
Br
O
Me
NO_2
(14) R=Br
(15) R=Me
R
Br
Br
Br
O
Me
ONO
(16) R=Br
(17) R=Me
O_2N-NO_2
O
H
O
Br
Br
R
Me
Br
(18a) R=Br
(19a) R=Me
R
Br
Br
Br
O
Me
OH
(18) R=Br
(19) R=Me
N_2O_4
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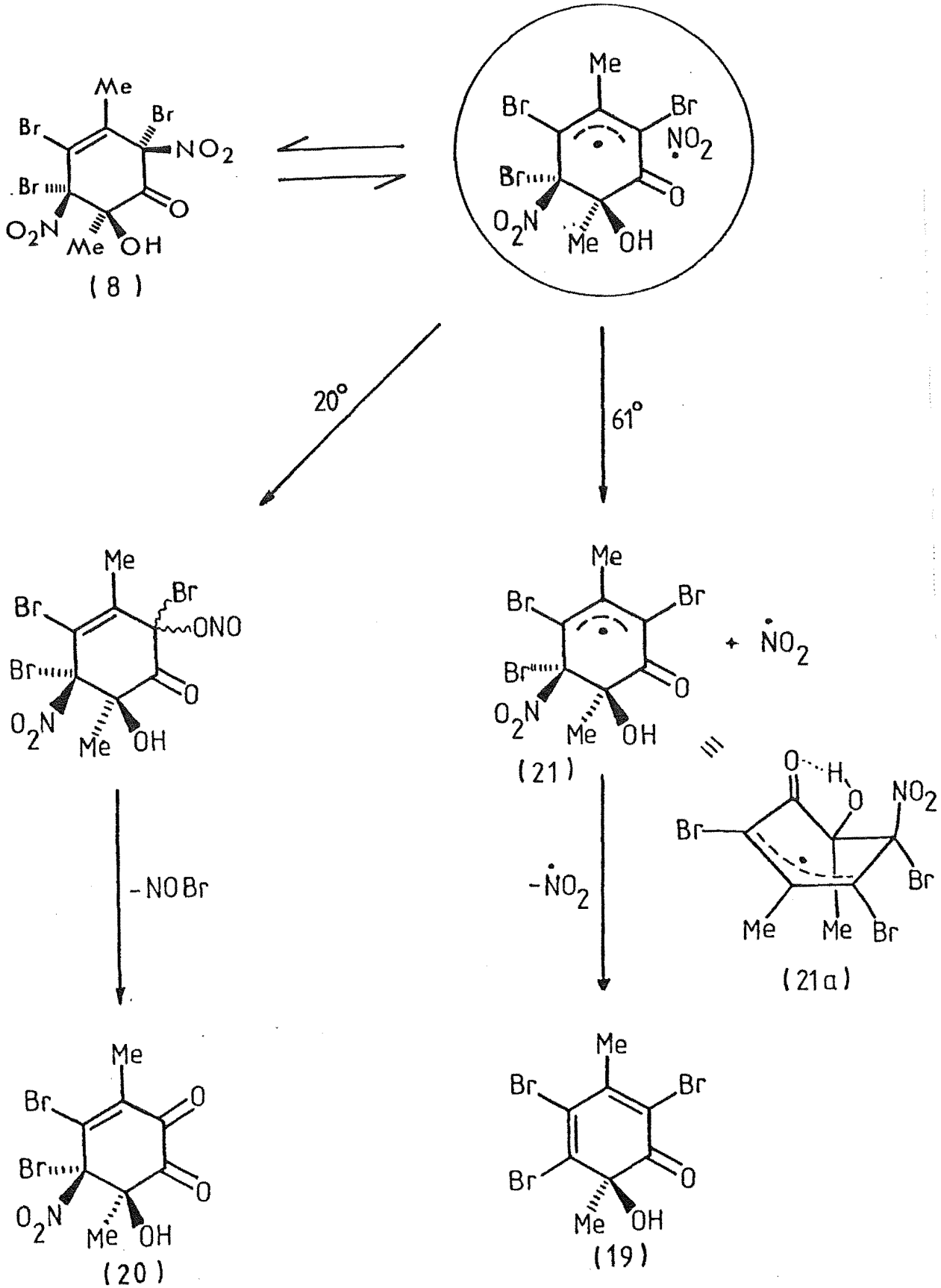
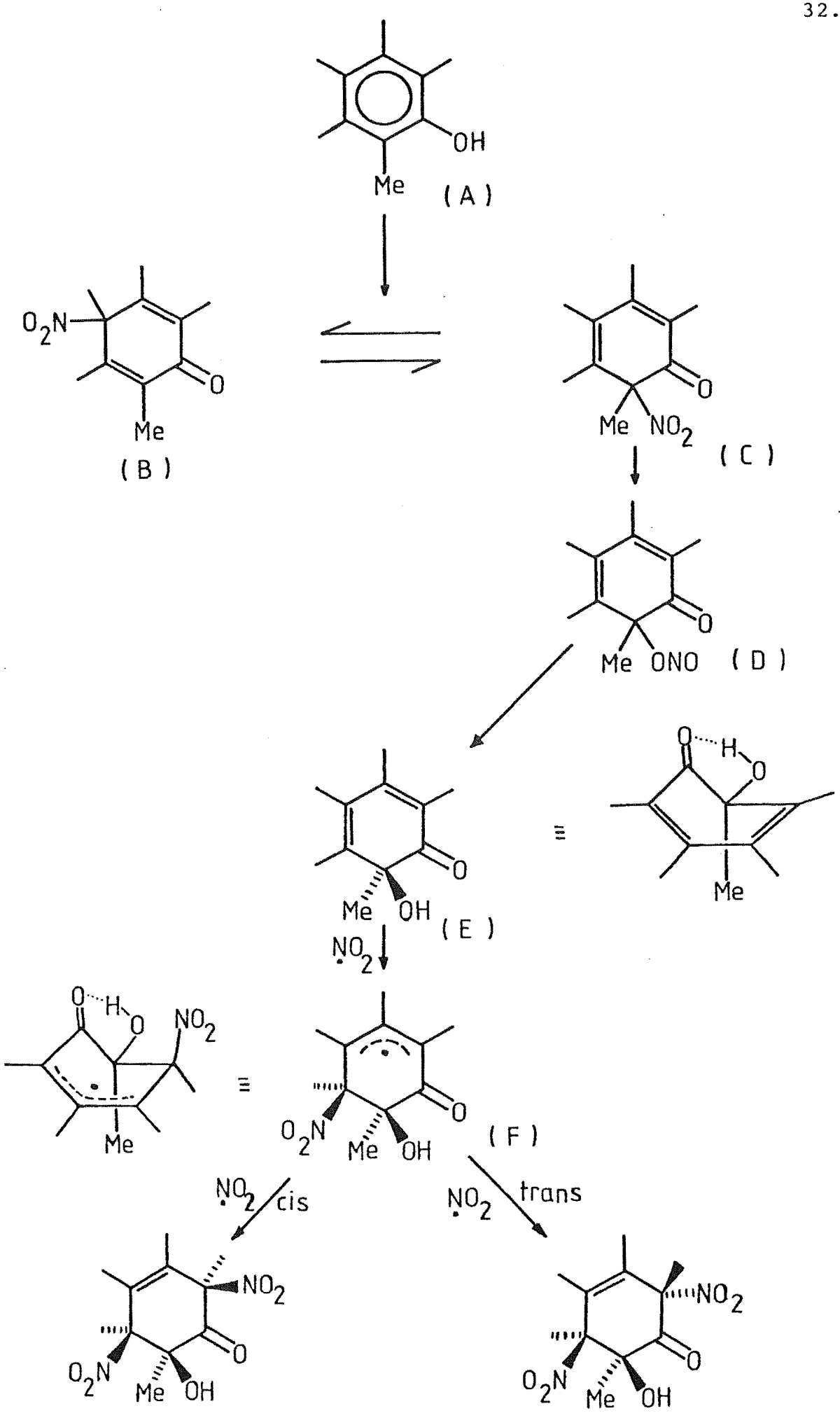
NO_2
Br
O
O_2N
Me
OH
(10) R=Br
(8) R=Me

SCHEME 4 .



SCHEME 5 .


OH
Me
(A)
O_2N
O
Me
(B)
Me NO_2
(C)
Me ONO
(D)
O···H
O
Me OH
(E)
≡
Me
NO_2
O···H
O
NO_2
≡
Me
O_2N
Me OH
(F)
NO_2 cis
NO_2 trans
NO_2
O_2N
Me OH
NO_2
O_2N
Me OH

SCHEME 6.

CHAPTER 2

NITRATION OF 1,3,5-TRICHLORO-2,4,6-TRIMETHYLBENZENE: ACYLOIN REARRANGEMENT STUDIES OF 6-HYDROXY-2,5-DINITROCYCLOHEX-3-ENONES

2.1 INTRODUCTION

Suzuki, Maruyama and Hanafusa have reported[41] the nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32), using fuming nitric acid in dichloromethane, to give the 4-hydroxydienone (33) and two further carbonyl compounds assigned structures (34) and (35) (Refer Scheme 7*). The 4-hydroxydienone (33), presumably formed from the corresponding 4-nitro compound (36) either in the reaction or, more likely, during the isolation procedure, was well-characterised and its formation satisfactorily accounted for by the suggested mechanism (Scheme 7).[41] In contrast, the evidence offered in support of structures (34) and (35) for the further two carbonyl compounds is not convincing.

Apart from mechanistic concerns regarding the formation of the intermediate (37) by the proposed 1,2-methyl shift and the lack of satisfactory analytical data for the compound assigned structure (34), the interpretation of the spectroscopic evidence was questionable. In particular, for the compound assigned structure (35), ν_{CO} 1750cm^{-1}, the infrared band frequency was attributed to the presence of a *gem*-dinitro functionality adjacent to the carbonyl group. Comparing this with recently reported[40,42] infrared data for structurally analagous compounds reveals a discrepancy.

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* Reaction Schemes as foldouts at end of Experimental Section.

For the known *gem*-dinitroketone (38) (Refer Block B*), the infrared carbonyl stretching frequency is 1770 cm^{-1},[42] compared with (39), ν_{CO} 1758 cm^{-1} [42]; (40), ν_{CO} 1755 cm^{-1} [42]; (29), ν_{CO} 1750 cm^{-1} [40]; and (30), ν_{CO} 1758 cm^{-1} [40]. On the basis of such a comparison it seemed probable that the compound assigned structure (35) had either a *gem*-chloronitro or a *gem*-methylnitro system adjacent to the carbonyl group, and not a *gem*-dinitro system. Also, the infrared carbonyl stretching frequency for the compound assigned structure (34), ν_{CO} 1715^{-1}, did not seem reasonable for a six-membered ring ketone flanked by two chlorine atoms and a nitro function. The similarity of the infrared stretching frequency with that reported[37,38] for the cyclopentene derivatives (9) and (11) (Block B) (obtained by base-catalysed acyloin rearrangement of the respective cyclohex-3-enones), ν_{CO} 1725 cm^{-1}, 1716 cm^{-1} respectively, suggested that the compound assigned structure (34) had a similar cyclopentene structural feature.

Nitration of 3,5-dichloro-2,4,6-trimethylphenol (41)[43] with fuming nitric acid in dichloromethane has been shown to give a mixture of the two C2-epimeric hydroxydinitrocyclohex-3-enones (42) and (43) (Block C); compound (42) was identical, with respect to its spectroscopic data and physical properties, to the material (35) isolated by Suzuki *et.al.*[41] from the nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32). The assignment of structures for the two hydroxydinitrocyclohex-3-enones (42) and (43) forms part of this present work, as will be demonstrated below. In view of the evidence presented above, the nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32) was repeated in order

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* Diagram Blocks as foldouts at end of Experimental Section

to complete the characterisation of the two compounds (42) and (43). In the event, nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32) also gave only the two C2-epimeric hydroxydinitrocyclohex-3-enones (42) and (43). A subsequent study of the base-catalysed acyloin rearrangements of these two compounds was performed in order to account more satisfactorily for the compound assigned the structure (34) by Suzuki *et.al.*[41]

2.2 DISCUSSION: THE NITRATION OF 1,3,5-TRICHLORO-2,4,6-TRIMETHYLBENZENE WITH FUMING NITRIC ACID IN DICHLOROMETHANE

Nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32) with fuming nitric acid in dichloromethane for 65h, and removal of the nitric acid and dichloromethane under reduced pressure, gave a crude product shown by ^{1}H n.m.r. to consist of a mixture of only two compounds (*c.*1:1). These compounds, cyclohex-3-enones (42) and (43) (Refer Block C for structures) were isolated by fractional crystallisation of the crude product from dichloromethane/pentane mixtures and were shown to be identical with the products obtained by similar nitration of 3,5-dichloro-2,4,6-trimethylphenol (41).[43]

The structures of compounds (42) and (43) were assigned by analogy with previously characterised hydroxydinitro-cyclohex-3-enones[37,38,40,42] and on the basis of their spectroscopic data (Refer Experimental). The less soluble compound (42) was assigned the *cis*-dinitro structure, initially on the basis of the relative infrared carbonyl stretching frequencies of the compound (42), ν_{CO} 1750 cm^{-1}, and (43), ν_{CO} 1760 cm^{-1}. These values compare well with the

data for the epimeric tribromodinitroketones (29), ν_{CO} 1750 cm^{-1}, and (30), ν_{CO} 1758 cm^{-1} (Refer Block C), the configurations of which had been previously established by X-ray crystal structure analysis.[40] Although the ^{13}C n.m.r. spectra could not be obtained for either of the dinitroketones (42) or (43), the remaining spectroscopic data were consistent with the assigned structures. Subsequently, an X-ray crystal structure analysis of the acyloin rearrangement product (44) (See Section 2.3.2 below), formed from the dichlorodinitroketone (43), revealed that it had the *trans*-dinitro stereochemistry; as the acyloin rearrangement of (43) does not involve the C2 or C5 atoms, or their substituents, the 2,5-dinitro stereochemistry of each ketone (42) and (43) is certain.

The *cis*-dinitroketone (42) gave spectroscopic data essentially identical with that reported by Suzuki *et.al.*[41] for the compound claimed to have the *gem*-dinitroketone structure (35), indicating that the previous prediction (Section 2.1) of a *gem*-methylnitroketone structure was indeed correct. No evidence was found among the nitration products for the presence of either the 4-hydroxydienone (33) or the compound (34) reported by Suzuki *et.al.*.[41] The absence of the 4-hydroxydienone (33) is readily explained in terms of the more complete conversion of the 4-nitrodienone intermediate (36) into the dichlorodinitroketones (42) and (43) in the longer reaction time of 65h, compared to Suzuki *et.al.* 16h.[41]

Apart from the extension of reaction time, mentioned above, the only significant difference in experimental technique between the reactions above and that reported by Suzuki *et.al.*[41] for the nitration of 1,3,5-trichloro-2,4,6-

trimethylbenzene (32) was in the work-up procedure employed. Given the known acyloin rearrangement of bromodinitroketones (8) and (10) on trituration with aqueous sodium carbonate solution to give cyclopentenol derivatives (9) and (11), it seemed conceivable that the second compound reported by Suzuki *et.al.*[41] might have been formed from one of the hydroxydinitroketones (42) or (43) during the aqueous sodium bicarbonate washing of the dichloromethane solution of the crude nitration product. For this reason, we examined the consequences of exposure of the hydroxydinitroketones (42) and (43) in dichloromethane solution to an aqueous solution of sodium bicarbonate. Under these mild reaction conditions, rearrangements of the hydroxydinitroketones (42) and (43) did occur, leading us to undertake a systematic study of the rearrangements of these and related hydroxydinitroketones.

2.3 DISCUSSION: THE BASE-CATALYSED ACYLOIN REARRANGEMENT OF 6-HYDROXY-2,5-DINITROCYCLOHEX-3-ENONES

The general reaction procedure[43] for the base-catalysed acyloin rearrangements of the 6-hydroxy-2,5-dinitrocyclohex-3—enones involves the vigorous agitation, in a suitable vessel (usually a small separatory funnel), of a two-phase system consisting of a solution of the hydroxydinitroketone in dichloromethane (2% w/v) and aqueous sodium bicarbonate solution (0.7% w/v; 25ml/g ketone) for the appropriate time period. Subsequent work-up procedures (See Experimental) gave a crude product which was separated into its components by fractional crystallisation.

2.3.1 BASE-CATALYSED ACYLOIN REARRANGEMENT OF *cis*-2,5-DINITROCYCLOHEX-3-ENONES

(For Reference, Structures and ^{1}H n.m.r. and infrared data for the *cis*-2,5-dinitrocyclohex-3-enones and their acyloin rearrangement products see Block D.)

a) Rearrangement of Tribromodinitroketone (8)

Brief treatment (30s) of the tribromodinitroketone (8), the stereochemistry of which had been established by X-ray crystal structure analysis,[37] with aqueous sodium bicarbonate gave a mixture of the two acyloin rearrangement products, cyclopentenol derivatives (9) and (45) (*c.* 4.5:1 by ^{1}H n.m.r.). The major product, readily separable from the mixture by fractional crystallisation, was the cyclopentenol derivative (9), the structure of which had been established previously by X-ray crystal structure analysis.[37]

Extended treatment (30 min) of the tribromodinitroketone (8) with aqueous sodium bicarbonate again gave a mixture of (9) and (45), but in a ratio (*c.* 2.9:1) more favourable for the isolation of the second product, cyclopentenol derivative (45). The assignment of structure (45) is based on the similarity of the spectroscopic data of compounds (9) and (45) plus the known stereochemical features of the acyloin rearrangement process. As the acyloin rearrangement of hydroxydinitroketone (8) does not involve the C2 or C5 atoms, or their substituents, the only possible difference between compounds (9) and (45) must involve the orientation of the Cl substituents, a

stereochemical feature that arises directly from the ring contraction process (Refer Scheme 8). Although satisfactory ^{13}C n.m.r. data could not be obtained for compound (45), the remaining spectroscopic data were consistent with the assigned structure.

In the ^{1}H n.m.r. spectra the acetyl protons for compound (45) (δ2.64) were markedly deshielded relative to the Cl-epimer (9) (δ2.37) (Refer Block D and Experimental). A similar deshielding was observed for the hydroxyl proton in compound (45) (δ5.7) relative to that for compound (9) (δ4.6). These observations led us to consider the possible use of the acetyl and hydroxyl proton ^{1}H n.m.r. spectroscopic parameters as a basis for the assignment of Cl stereochemistry in related cyclopentenol derivatives. In the event, this correlation was found to be a convenient and reliable method of establishing the Cl stereochemistry in the cyclopentenol derivatives containing the *cis*-2,5-dinitro structural feature.

b) Rearrangement of Tribromodinitroketone (29)

Brief treatment (30s) of the tribromodinitroketone (29), whose structure had been established previously by X-ray crystal structure analysis,[40] with aqueous sodium bicarbonate gave an incomplete rearrangement of the ketone (29) into a mixture (*c.* 1:1:1) of the tribromodinitroketone (29) and the two acyloin rearrangement products, cyclopentenol derivatives (46) and (47). All three compounds were separable by fractional crystallisation. This incomplete rearrangement is presumably due to the reduction in the driving force for acyloin rearrangement

because of the stabilising effect of the electron-donating C2-methyl group on the substituted cyclohex-3-enone (29). The spectroscopic data for the two acyloin rearrangement products (46) and (47) fully support the assigned structures (See Experimental) and fit the pattern of ^{1}H n.m.r. spectra for the C1-epimers noted in part (a) above.

c) Rearrangement of Tetrabromodinitroketone (10)

Very brief treatment (*c.* 10s), or more prolonged treatment (5 min), of the tetrabromodinitroketone (10)[38] with aqueous sodium bicarbonate gave a mixture of the acyloin rearrangement products, cyclopentenol derivatives (11) and (48) (*c.* 1:1 by ^{1}H n.m.r.), which were separated by fractional crystallisation. The less soluble compound (11) was identical in all respects with the material previously formed from the tetrabromodinitroketone (10) by trituration of the solid ketone with aqueous sodium carbonate solution.

The second acyloin rearrangement product, cyclopentenol derivative (48), gave, as expected, a ^{13}C n.m.r. spectrum whose relative simplicity pointed to a plane of symmetry in the molecule; in addition, the remaining spectroscopic data were also consistent with the assigned structure (See Experimental). In particular, the ^{1}H n.m.r. data for the compound (48), when compared to that for compound (11), fit the pattern noted in part (a), above, for compounds (9) and (45), thus supporting the assignment of structure (48) as the C1-epimer of compound (11).

An interesting feature of compound (48), as in the stereochemically related compounds (45) and (47), is the appearance of the infrared carbonyl stretching band as a double peak and the broadening of the infrared hydroxyl stretching band confirming the presence of strong carbonyl-hydroxyl hydrogen bonding in the solid state.

d) Rearrangement of Dichlorodinitroketone (42)

Brief treatment (5 min) of the dichlorodinitroketone (42) with aqueous sodium bicarbonate resulted in incomplete conversion of the ketone (42) into a single acyloin rearrangement product, cyclopentenol derivative (49) (mixture; *c.* 5:4, ketone (42): compound (49)).[43] This compound, separated from ketone (42) by fractional crystallisation and assigned structure (49), gave analytical data for a molecular formula $C_9H_{10}Cl_2N_2O_6$. In addition, it had physical and spectroscopic data identical with that reported for the material assigned structure (34) by Suzuki *et.al.*,[41] except for the ^1H n.m.r. value for the C2-methyl protons (See Experimental). It appears, therefore, that the compound reported by Suzuki *et.al.*[41] as structure (34) is the acyloin rearrangement product (49) and that it was formed from the dichlorodinitroketone (42) on the washing of a dichloromethane solution of the crude product with aqueous sodium bicarbonate solution.

Extended treatment (30 min) of the dichlorodinitro-ketone (42) with aqueous sodium bicarbonate gave a mixture (*c.* 1:1:1.5) of the ketone (42) and the two acyloin rearrangement products, cyclopentenol derivatives (49) and (50). All three compounds were separable by fractional

crystallisation. Although satisfactory ^{13}C n.m.r. spectroscopic data could not be obtained for compound (50), the remaining spectroscopic data were consistent with the assigned structure (See Experimental), and the ^{1}H n.m.r. data for the C1-epimers (49) and (50) fit the pattern developed above in parts (a)-(c). Again it appears that the presence of the C2-methyl group in the ketone (42) has the effect of reducing the driving force for its conversion into the cyclopentenol derivatives (49) and (50). From the experiments above, it is clear that compound (49) is the product of kinetic control in the acyloin rearrangement of the dichlorodinitroketone (42).[43]

2.3.2 BASE-CATALYSED ACYLOIN REARRANGEMENT OF *trans*-2,5-DINITROCYCLOHEX-3-ENONES

(For Reference, Structures and ^{1}H n.m.r. and infrared data for the *trans*-2,5-dinitrocyclohex-3-enones and their acyloin rearrangement products see Block E)

a) Rearrangement of Dichlorodinitroketone (43)

Brief treatment (1 min) of the dichlorodinitroketone (43) with aqueous sodium bicarbonate gave an incomplete conversion of the ketone (43) into a mixture (*c.* 5:5:3 by ^{1}H n.m.r.) of the ketone (43) and the two acyloin rearrangement products, cyclopentenol derivatives (51) and (44); the cyclopentenol derivative (51) was isolated by fractional crystallisation. The spectroscopic data for compound (51) were entirely consistent with the assigned structure.

More prolonged treatment (30 min) of the

dichlorodinitroketone (43) with aqueous sodium bicarbonate gave a mixture (*c.* 1:1:2 by ^{1}H n.m.r.) of the ketone (43) and the two cyclopentenol derivatives (51) and (44) from which the cyclopentenol derivative (44) was isolated by fractional crystallisation. Again, the spectroscopic data for compound (44) were entirely consistent with the assigned structure.[43]

In the ^{1}H n.m.r. spectra the acetyl protons for compound (44) (δ2.24) were markedly shielded relative to the Cl-epimer (51) (δ2.45) (Refer Block E and Experimental). A deshielding, similar to that observed for the *cis*-2,5-dinitro cyclopentenol derivatives in Section 2.3.1, was observed for the hydroxyl protons in compounds (44) (δ5.4) and (51) (δ4.3).

Even though the spectroscopic data for compounds (51) and (44) were in accord with the assigned structures, these data did not allow unequivocal assignment of the stereochemistry at C-1 in the two cyclopentenol epimers (51) and (44). The structure of compound (44) was therefore established by X-ray crystal structure analysis. A perspective drawing of the structure (44) is presented in Figure 1* with corresponding atomic coordinates in Table 1.* For compound (44) the cyclopentene ring is close to being planar and there is evidence for intramolecular carbonyl-hydroxyl hydrogen bonding. In the structure the O(1)-O(6) distance is 2.562(4)Å, the HO(1)-O(6) distance is 1.92(6)Å, the O(1)-HO(1)-O(6) angle is 133(5)° and the O(6)-C(6)-C(1)-O(1)-HO(1) system is nearly planar.[43] The point of closest intermolecular approach in

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* Figures and Tables as foldouts at end of Experimental Section.

the crystalline state is between O(6') and HO(1) (2.27Å); no other intermolecular distance is less than 2.57Å and there is no extended hydrogen bond network in the crystal.

Given the established structure of compound (44), and the fact that the acyloin rearrangement of dichlorodinitroketone (43) does not involve the C2 or C5 atoms or their substituents, the *trans*-2,5-dinitro structure for dichlorodinitroketone (43) is confirmed. Similarly, the inclusion of the *cis*-Cl-hydroxyl, C5-nitro structural feature in compound (44) is confirmed and hence the relative stereochemistry of the cyclopentenol derivative (51) is defined by exclusion.

b) Rearrangement of Tribromodinitroketone (30)

Brief treatment (30s) of the tribromodinitroketone (30), the structure of which had been determined previously by X-ray crystal structure analysis,[40] with aqueous sodium bicarbonate gave a mixture (*c*. 1:1.7 by ^{1}H n.m.r.) of the two acyloin rearrangement products, cyclopentenol derivatives (52) and (53); these compounds were separated by fractional crystallisation. The structures of these compounds were assigned by comparison of their spectroscopic data (particularly ^{1}H n.m.r. data) with those of the corresponding dichlorodinitro compounds (51) and (44). The spectroscopic data are entirely consistent with the assigned structures (52) and (53) and fit the pattern of ^{1}H n.m.r. spectra for the Cl-epimers noted in part (a) above.

2.3.3 CORRELATION OF STRUCTURAL FEATURES WITH SPECTROSCOPIC DATA FOR *cis*- AND *trans*-2,5-DINITROCYCLOHEX-3-ENONES

At this point, some comment can be made on the ^{1}H n.m.r. data for the *cis*-dinitrocyclohex-3-enones and their derived acyloin rearrangement products which are given in Block D, and the corresponding *trans*-dinitrocyclohex-3-enones and their derived acyloin rearrangement products given in Block E. Notable for the *cis*-dinitrocyclopentenol derivatives is the marked downfield shift of the acetyl methyl protons (Δ0.21-0.29) when the acetyl group is *trans*- rather than *cis*- to the nitro functions. A similar downfield shift of the acetyl methyl protons (Δ0.13-0.21) is observed for the *trans*-dinitrocyclopentenol derivatives when the acetyl group is *trans*- rather than *cis*- to the C2-nitro function. For the cyclopentenol derivatives having a C2-methyl group, the chemical shift of this C2-methyl group is dependent on whether it is *cis*- (δ1.90-1.97) or *trans*- (δ1.74-1.78) to the C1-hydroxyl group.

2.3.4 DISCUSSION: EQUILIBRIA IN THE BASE-CATALYSED ACYLOIN REARRANGEMENT OF 6-HYDROXY-2,5-DINITROCYCLOHEX-3-ENONES

In order to investigate the reversibility of the base-catalysed acyloin rearrangement of the 6-hydroxy-2,5-dinitrocyclohex-3-enones to give the C1-epimeric cyclopentenol derivatives, the dichlorodinitrocyclopentenol derivatives (49) and (51) were treated with aqueous sodium bicarbonate as for the rearrangement of ketones (42) and (43) respectively (Refer Sections 2.3.1, 2.3.2).[43] In

each case a mixture of the corresponding substituted cyclohex-3-enone (42) or (43) and the two Cl-epimeric cyclopentenol derivatives (49) and (50) or (51) and (44) was obtained.[43]

The ratio of products obtained for the reaction of compound (49) for 5 min [(42):(49):(50), *c.* 1:1:1.5] was similar to the ratio of products for the relatively long-term (30 min) treatment of the cyclohex-3-enone (42) on a larger scale (See Experimental). This apparent disparity in the rate of equilibration has limited significance because it was found subsequently that the rate of rearrangement in the dichloromethane/aqueous sodium bicarbonate two-phase system was scale-dependent; the higher rate of conversion in small scale reactions presumably due to more efficient mixing.

Similarly, brief treatment (1 min) of the *trans*-dinitro cyclopentenol derivative (51) with aqueous sodium bicarbonate on a small scale gave a product mixture relatively rich in compound (51) and the cyclohex-3-enone (43) [(43):(51):(44), *c.* 5:5:4].

These results are consistent with an equilibration as shown in Scheme 9 for the system (49)⇌(42)⇌(50) and Scheme 10 for the system (51)⇌(43)⇌(44). It should be noted that although each rearrangement process involves the conversion of an α-keto alkoxide ion into an isomeric α-keto alkoxide ion, Schemes 9 and 10 have been presented in order to highlight the stereochemical features of the rearrangements. Formation of the dichlorodinitrocyclohex-3-enone (42) from the cyclopentenol derivative (49), or indeed from the cyclopentenol derivative (50), requires

the acetyl group conformation in each case to be as indicated in Scheme 9. Also, for the formation of the cyclopentenol derivative (49) from the dichlorodinitro-cyclohex-3-enone (42) reaction must occur with the molecule in a conformation resembling (42a), while cyclopentenol derivative (50) formation requires reaction to be possible in a conformation resembling (42b). Similarly, formation of the dichlorodinitrocyclohex-3-enone (43) from the cyclopentenol derivative (51), or indeed from the cyclopentenol derivative (44), requires the acetyl group conformation in each case to be as indicated in Scheme 10. For the formation of the cyclopentenol derivative (51) from the dichlorodinitro-cyclohex-3-enone (43) reaction must occur with the molecule in a conformation resembling (43a), while cyclopentenol derivative (44) formation requires reaction to be possible in a conformation resembling (43b).

It is notable that the C6-epimeric cyclohex-3-enone (54) was not detected in the study of the equilibrium (49)$\rightleftharpoons$(42)$\rightleftharpoons$(50). This result implies that the rearrangement of cyclopentenol derivatives (49) and (50) in conformations (49a) and (50a) respectively either do not occur, or occur only very slowly (Refer Scheme 11). Alternatively, the C6-epimeric cyclohex-3-enone (54) may be thermodynamically less stable than the cyclohex-3-enone (42) in the dichloromethane/aqueous sodium bicarbonate system and so not be present in sufficient concentration for its detection. No evidence for the formation of compounds analagous to the C6-epimeric cyclohex-3-enone (54), in either the *cis*- or *trans*-dinitro series, was found in

the base-catalysed acyloin rearrangement studies.

Also of interest is the observation that the conformations of the cyclopentenol derivatives (49) and (50) required for the observed base-catalysed acyloin rearrangements to occur correspond to the conformations in which these compounds exist in the solid state. The conformation of cyclopentenol derivative (50) required for the rearrangement is similar to the conformation already established for cyclopentenol derivative (44), the cyclopentenol derivative C2-epimeric to (50), in the solid state.[43] Although the conformation of cyclopentenol derivative (49) itself has not been determined, the structure of cyclopentenol derivative (9), containing the same stereochemical features as (49), has been determined;[37] the acetyl group has, in this case, the same orientation as that required in Scheme 9 for the rearrangement to take place. This conformational similarity between the solid state and solution phase is of great importance, especially when X-ray crystal structure analysis is used to correlate structure with reactivity or structure with spectroscopic parameters. The importance of this relationship will become more apparent in subsequent chapters.

2.4 DISCUSSION: FORMATION OF A C6-EPIMERIC CYCLOHEX-3-ENONE FROM CYCLOPENTENOL DERIVATIVE (49)

The cyclohex-3-enones derived from fuming nitric acid nitration of halogenated polysubstituted phenols have all been shown to have *cis*-C6-hydroxy, C5-nitro stereochemistry;[37,38,40,42,43] this stereochemical feature arises during the addition of nitrogen dioxide to the corresponding

6-hydroxydienone. The addition of nitrogen dioxide to the dienone system is envisaged as occuring by homolytic, two-step, 1,4-addition initiated by attack of a nitrogen dioxide radical ($\dot{N}O_2$) at C5. This attack occurs on the less-hindered face of the dienone system, the conformation of which is determined by intramolecular carbonyl-hydroxyl hydrogen bonding (Refer Scheme 6, Introduction). In none of the nitration reactions thus far studied had a cyclohex-3-enone with *trans*-C6-hydroxyl, C5-nitro stereochemistry been isolated or detected.

Similarly, in the base-catalysed acyloin rearrangement studies of these *cis*-C6-hydroxy, C5-nitrocyclohex-3-enones[43] (Sections 2.3.1-2.3.3), the cyclopentenol derivatives formed by the ring contraction-rearrangement have been shown to undergo ring expansion-rearrangement only in particular conformations, such that the cyclohex-3-enone generated retains the *cis*-C6-hydroxy, C5-nitro stereochemistry (Refer Schemes 9 and 10).

The lack of evidence for *trans*-C6-hydroxy, C5-nitro compounds in the base-catalysed acyloin rearrangement studies (Sections 2.3.1-2.3.3) could be the result of either of two possible influences (as discussed in Section 2.3.4): (i) the failure of the cyclopentenol derivatives to attain or react in conformations analagous to (49a) or (50a) (Scheme 11) or (ii) the C6-epimeric cyclohex-3-enones conformationally analagous to compound (54) may be thermodynamically less stable in the dichloromethane/aqueous sodium bicarbonate system than the *cis*-C6-hydroxy, C5-nitro cyclohex-3-enones conformationally analagous to (42) or (43).

During the intensive study of the base-catalysed acyloin rearrangement of substituted cyclohex-3-enones (Sections 2.3.1-2.3.2),[43] ^{13}C n.m.r. spectra were routinely collected as part of the total spectroscopic data on the cyclopentenol derivative rearrangement products. The majority of the cyclopentenol derivatives gave ^{13}C n.m.r. spectra which indicated the presence of a single compound, as would be expected. However, when the cyclopentenol derivative (50) was dissolved in deuterioacetone at -78° and the ^{13}C and ^{1}H n.m.r. spectra obtained at -25°, both techniques revealed, surprisingly, the presence of two species (*c.* 3:2 by ^{1}H n.m.r.).[45] Raising the temperature of the solution to 30° had no apparent effect on the ratio of the two compounds. Removal of the solvent at 20° under reduced pressure gave a crude product, shown by ^{1}H n.m.r. ($CDCl_3$) and infrared spectra to be a mixture of the cyclopentenol derivative (50), as the major component, and the C6-epimeric 6-hydroxy-6-methyl-2,5-dinitrocyclohex-3-enone (54), as the minor component.[45] Pure samples of each of compound (50) and compound (54) were obtained from the mixture by fractional crystallisation.

The structure of compound (54) was established by X-ray crystal structure analysis. A perspective drawing of the structure (54) is presented in Figure 2 with corresponding atomic coordinates in Table 2. The spectroscopic data for compound (54) are in accord with its established structure (See Experimental). In structure (54) the cyclohex-3-enone ring system is in a slightly-flattened half-chair conformation [ring torsional angles:

C(4)-C(3)-C(2)-C(1) -10(2)°, C(3)-C(4)-C(5)-C(6) -19(2)°], in contrast to the twist-boat conformations for the C2-epimeric tribromodinitroketones (29) and (30).[40] In structures (29) and (30), the O(1)-O(6) distances were 2.65Å and the C(1)-O(1) and C(6)-O(6) bonds were close to *syn*-coplanar, indicating intramolecular carbonyl-hydroxyl hydrogen bonding. For compound (54), the C6-hydroxyl group is in an axial orientation, intramolecular carbonyl-hydroxyl hydrogen bonding is absent and no evidence was found for intermolecular hydrogen bonding involving the C6-hydroxyl group. In contrast, the stereochemical relationship (pseudoaxial) between the C5-nitro bond and the ring system for compound (54) is similar to that found for the C2-epimeric dinitroketones (29) and (30)[40] and the tribromodinitroketone (8).[37]

In deuteriochloroform solution the C6-epimeric cyclohex-3-enone (54) was stable, but in deuterioacetone it was rapidly converted into an equilibrium mixture of the ketone (54) and the cyclopentenol derivative (50). When a dichloromethane solution of the C6-epimeric dinitrocyclohex-3-enone (54) was treated with aqueous sodium bicarbonate (as for the general procedure, Section 2.3.1), it was converted into a mixture (*c.* 1:1:1) of the dinitroketone (42) and the two cyclopentenol derivatives (49) and (50);[43,45] the C6-epimeric cyclohex-3-enone (54) could not be detected in the crude product (by ^{1}H n.m.r.). These results indicate that, although the C6-epimeric cyclohex-3-enone (54) is comparable in stability with the cyclopentenol derivative (49) in acetone solution, in the dichloromethane/aqueous sodium bicarbonate system it is

thermodynamically less stable than the isomeric compounds (42), (49) and (50).[45]

An interesting feature of the rearrangement of compound (54) in acetone is that the equilibrium established is between compound (54) and compound (50) only; compound (49) is not formed. This would imply, referring to Scheme 12, that compound (54) exists or reacts, in acetone solution, in conformation (54a) only, rearranging to give compound (50). In conformation (54a) the C6-hydroxyl group, occupying a pseudoaxial position, can readily hydrogen-bond to an acetone solvent molecule. In the alternative conformation (54b), the conformation required to give rise to cyclopentenol derivative (49), the C6-hydroxyl group is in a position *gauche* to the C5-chlorine atom. In conformation (54b), hydrogen bonding between the C6-hydroxyl group and an acetone molecule would give rise to unfavourable interactions between the solvent molecule and the C5-chlorine atom, making conformation (54b) much less favourable, energetically, than conformation (54a).

During the entire study of the base-catalysed acyloin rearrangements of substituted dinitrocyclohex-3-enones,[43] only compound (50) was observed to undergo this unusual isomerisation in acetone solution. Given that the cyclopentenol derivatives (9),(11),(44),(45),(46),(47),(48), (49),(51),(52) and (53) (Sections 2.3.1-2.3.2) include compounds isomeric at C1 and C2 with compound (50), it is clear that the rearrangement in acetone is highly specific with respect to structural and stereochemical requirements.

CHAPTER 3

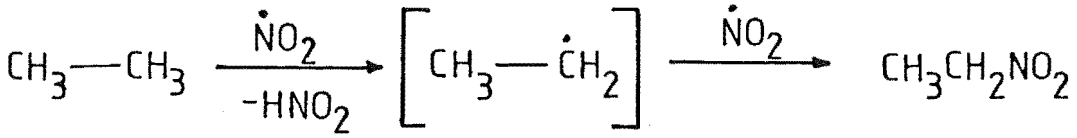
NITRATION OF POLYSUBSTITUTED HALOGENATED PHENOLS WITH NITROGEN DIOXIDE

3.1 INTRODUCTION

Conventional electrophilic nitration of organic compounds can be achieved by many methods. These include reaction of the substrate with nitric acid in sulphuric acid, with nitric acid metal salts, mixed anhydrides or nitrate esters (all catalysed by sulphuric acid or Lewis acids),[46a,b,c] or with metal salts catalysed by resin-acids.[46d]

It is, however, evident in the literature that nitration is simply not confined to electrophilic attack. Significant examples of free-radical nitration are many and varied.[47] For example, nitration of aromatic compounds can be achieved by the lower oxides of nitrogen, N(III) and N(IV),[47a,b] and the kinetics of these reactions indicate that they involve hydrogen abstraction.

Similarly, the rate of nitration of alkanes such as ethane and propane with nitrogen dioxide, in the gas phase, has been shown to be dependent on hydrogen abstraction by nitrogen dioxide as the initiating step.[47c]



Dinitrogen tetroxide (N_2O_4), the dimeric form of nitrogen dioxide ($\dot{N}O_2$), dissociates readily at room temperature to an equilibrium mixture of nitrogen dioxide and dinitrogen tetroxide. In the gas phase, the equilibrium constant K_c^{298}, for the equilibrium:

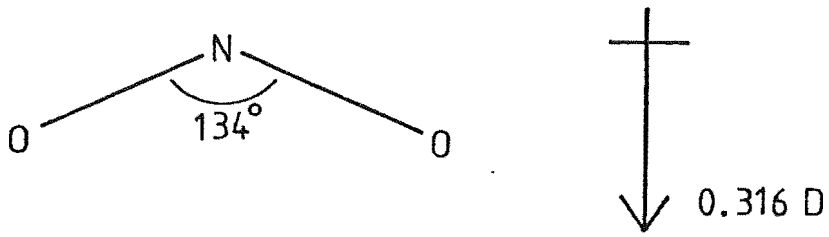
$$N_2O_4 \underset{}{\overset{K_c^{298}}{\rightleftharpoons}} 2NO_2$$

has been measured as 1.51×10^{-1} mol l^{-1} [48]. In non-coordinating solvents such as cyclohexane and carbon tetrachloride this value is reduced to 1.77×10^{-4} mol l^{-1}, the greater stability of dinitrogen tetroxide in this case being due to a reduction in the entropy of dissociation with respect to the gas phase rather than a reduction in the enthalpy of dissociation.[49] A further reduction in K_c^{298} is observed in coordinating solvents such as acetonitrile (K_c^{298}(acetonitrile) 0.3×10^{-4} mol l^{-1}). This is attributable to association of the dinitrogen tetroxide species with the solvent, this fact being reflected in an increase in the enthalpy of dissociation of dinitrogen tetroxide in acetonitrile.[49]

The monomeric, unpaired-electron species, nitrogen dioxide ($\dot{N}O_2$) has been subjected to extensive electron-spin-resonance (e.s.r.) spectroscopy investigations with respect to the location of the unpaired-electron spin-density. These have included both solution studies[50] and studies of the radical "trapped" in various matrices.[51] Solution studies[50] in non-polar non-coordinating solvents, such as cyclohexane, have shown that

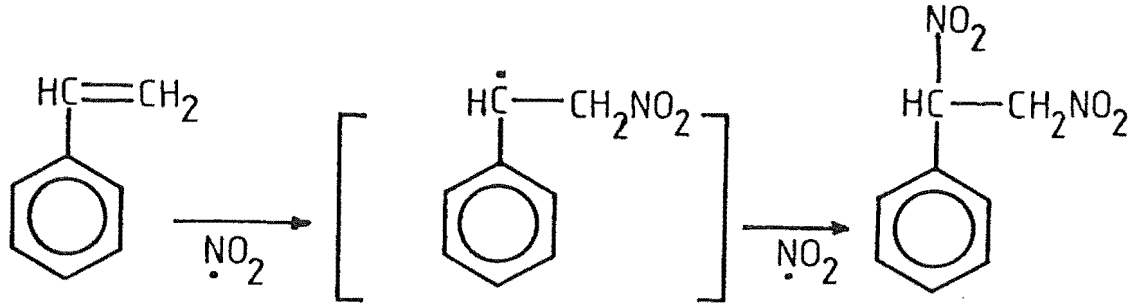
the unpaired-electron spin-density is distributed so that approximately 50% is located on the nitrogen atom, leaving about 25% of the spin-density on each oxygen atom. In addition, these studies have calculated the O-N-O bond angle in solution to be 132-134°[50a], not far removed from the gas phase electron diffraction value of 134°.[52] This extensive delocalisation of the unpaired-electron in nitrogen dioxide is a fundamental driving force in the dissociation of dinitrogen tetroxide.[50a]

In addition to its unpaired-electron character, nitrogen dioxide has a significant electric dipole moment of 0.316 D (1 Debye = 10^{-18} e.s.u. cm),[53] as compared with the dipole moment of water (1.85 D), the more electropositive nitrogen atom being the positive terminus of the dipole.



This dipole moment gives the nitrogen centre of the nitrogen dioxide radical significant electrophilic character, especially with respect to reactions involving electron-rich molecules such as aromatic nuclei or diene systems.

Addition of nitrogen dioxide to unsaturated organic systems, especially carbon-carbon double bonds and aromatic nuclei, has been shown[54] to involve free-radical intermediates. For example, the reaction of styrene with nitrogen dioxide has been demonstrated by e.s.r. spectroscopy to involve the intermediacy of a free-radical rather than a pi-complex of any kind.[47d]



The reaction of nitrogen dioxide with conjugated dienone systems[38,39,40] has already been demonstrated in Chapter 1. The proposed mechanism[38] for the addition is consistent with a 1,4-homolytic addition of nitrogen dioxide involving a delocalised radical intermediate.

Nitrogen dioxide reacts with phenols by abstraction of the labile phenolic hydrogen to give phenoxy radicals. These highly delocalised radicals have been demonstrated, by e.s.r. spectroscopy, as intermediates in the reactions of 2,4,6-tri-t-butylphenol[55] and 2,6-di-t-butyl-4-methylphenol[56] with nitrogen dioxide.

Phenoxy radicals can be generated from the corresponding phenols by a variety of methods, including oxidation of the phenol in non-polar solvent with silver (II) oxide or lead dioxide[57] or, more commonly, oxidation of the phenol in benzene with alkaline potassium ferricyanide solution.[55] Generally, the more stable phenoxy radicals are those with a 2,4,6-trisubstitution pattern and especially stable are those radicals with bulky 2,6-substituents which possess no α-hydrogens. For example, 2,4,6-tri-t-butylphenoxy radical is especially stable, giving intense blue-coloured solutions which are stable over long periods.[55,58]

E.S.R. spectroscopy measurements of phenoxy radicals[57]

have been used to determine the proportion of the unpaired-electron spin-density at the various ring positions. Maximum electron density occurs at the carbon-4 position, with lesser amounts at the carbon-2, carbon-6, and carbon-1, oxygen positions, and a "negative" spin-density at the carbon-3 and carbon-5 positions. This determination fits with the observed frequency-of-attack at the various ring positions on the phenoxy radical; C4>C2,C6>C1,O≫C3,C5.

Although phenoxy radicals are of reasonable stability, they are extremely reactive with other unpaired-electron species. For example, 2,4,6-tri-t-butylphenoxy radical is very stable but it reacts rapidly in solution with unpaired-electron species such as nitrogen dioxide.[55] In the absence of such unpaired-electron species less stable, less sterically hindered phenoxy radicals can dimerise to give stable compounds.[57d]

It has been shown[55,56] that the nitration of some phenols with nitrogen dioxide proceeds entirely by free-radical mechanisms and it has been demonstrated[59] that in the nitric acid nitration of alkanes, nitric acid itself is inert and serves only as a vehicle for nitrogen dioxide, the active nitrating species. With these observations in mind it does not seem unreasonable to suggest that the fuming nitric acid nitrations of polysubstituted phenols may proceed by free-radical mechanisms, at least for the latter steps of the reaction involving the conversion of cyclohexadienones to cyclohexenones, if not in entirety. In order to test such a hypothesis, it was decided to explore the reactions of the polysubstituted halogenated phenols (previously nitrated with fuming nitric acid) with nitrogen dioxide in suitable, non-polar solvents.

3.2 SYNTHESIS OF NITROGEN DIOXIDE

Pure nitrogen dioxide was prepared for use in a specially designed high-vacuum gas-line (Refer Figure 3*), consisting of a 5-litre round flask with a cold-finger side arm, a mercury manometer, gas inlet and a set of liquid air cooled gas traps. Pure, dry nitric oxide ($\dot{N}O$: Matheson & Co.) (5 litre-atmospheres was added to the main flask (previously evacuated by high-vacuum pumping for 1 h) and transferred by condensation at liquid air temperatures into the side arm. When the manometer indicated no residual pressure in the vacuum line (that is, all nitric oxide condensed), pure, dry oxygen (2.5 litre-atmospheres) was added rapidly to the main flask and the cold trap was removed from the side arm containing the condensed nitric oxide allowing the two gases to react. The main flask, sealed at Tap A (Refer Figure 3), was left overnight to allow the reaction to proceed to completion. The nitrogen dioxide thus formed was transferred by condensation at liquid air temperatures into a specially designed 1-litre flask (Refer Figure 4) where it was stored prior to use. During the transfer of nitrogen dioxide to the smaller flask, the crystalline material deposited in the cold-finger was colourless, indicating the presence of the dimeric dinitrogen tetroxide only. Other oxides of nitrogen, such as dinitrogen trioxide and dinitrogen pentoxide, are coloured and so their absence is implied. During the experimental work involving the use of nitrogen dioxide, the utmost care was taken to exclude atmospheric oxygen and water from the storage bulb.

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* Figures as foldouts at end of Experimental Section.

3.3 REACTIONS OF HALOGENATED POLYSUBSTITUTED PHENOLS WITH NITROGEN DIOXIDE

The general reaction procedure for these reactions was as follows: A suspension of the phenol in the chosen solvent was thoroughly purged of oxygen by bubbling through dry nitrogen for 5 min while the suspension was kept at approximately 10^{o}. The suspension of phenol was then saturated with gaseous nitrogen dioxide, obtained by warming the liquid nitrogen dioxide/dinitrogen tetroxide mixture in the storage flask to above the boiling point (21.2^{o}), and then left to stir, with an atmosphere of nitrogen dioxide maintained above the solution, for the appropriate time period. Excess nitrogen dioxide was then removed from the reaction system by a stream of dry nitrogen. Any precipitated products were removed by filtration through a sintered-glass funnel and the solvent was evaporated from the filtrate under reduced pressure at 20^{o}. Spectra of both precipitate and filtrate were obtained prior to any manipulations of the materials.

3.3.1 DISCUSSION: REACTIONS OF HALOGENATED POLYSUBSTITUTED PHENOLS (2),(5),(28) AND (41) AND 6-HYDROXYDIENONE (31) WITH NITROGEN DIOXIDE IN CYCLOHEXANE

Reaction of 2,3,4,5-tetrabromo-6-methylphenol (2) in cyclohexane with nitrogen dioxide, as described in the general procedure, was rapid and gave a precipitate identified as the *cis*-2,5-dinitrocyclohex-3-enone (10) (Refer Block A), identical in all respects to the nitric acid nitration product,[38] plus a residue shown to be primarily the *cis*-2,5-dinitroketone (10). The total accountable yield of compound (10) was 85%.[60]

Similar reaction of 2,4,5-tribromo-3,6-dimethylphenol (5) was again rapid, giving the corresponding *cis*-2,5-dinitrocyclohex-3-enone (8)[37] as a thick precipitate. The residue contained, in addition to compound (8), 2,5-dibromo-3,6-dimethylbenzo-1,4-quinone which is probably the result of oxidation of the 4-nitrodienone obtained from phenol (5) by nitrogen dioxide. No compound corresponding to the *trans*-dinitro form of compound (8) could be detected in the residue. The total accountable yield of compound (8) was 75%.[60]

Reaction of 3,4,5-tribromo-2,6-dimethylphenol (28) in cyclohexane with nitrogen dioxide was rapid and gave a mixture of the *cis*-(29) and *trans*-(30) hydroxydinitroketones identical with authentic materials derived from the nitric acid nitration of phenol (28).[40] The overall yields of these compounds (precipitate plus residue) were (29) 56% and (30) 31% respectively,[60] similar to the yields obtained from the nitration of the phenol (28) with fuming nitric acid in acetic acid ((29), 54%; (30), 30%).[40]

A short-term reaction (2h) of 3,5-dichloro-2,4,6-trimethylphenol (41) gave mainly the corresponding 4-nitrocyclohexa-2,5-dienone (36), a result in keeping with the short-term nitration of phenol (41) with fuming nitric acid in dichloromethane. Extension of the reaction time (88h) resulted in the formation of a mixture (*c.* 3:2, total precipitate plus residue) of the *cis*-(42) and *trans*-(43) dinitroketones, identical in all respects with authentic materials derived from the nitric acid nitration of phenol (41).[43] The residue also contained materials whose identity could not be established due to their unstable nature.[60]

For phenols (2), (5), (28) and (41) the products of reaction with nitrogen dioxide in cyclohexane are the same as

the products from nitration using fuming nitric acid in acetic acid. It was decided, therefore, to examine more closely the reactions of one of these phenols (28) with nitrogen dioxide in cyclohexane. When the reaction time was reduced to 1.5 min (from 2h), some unchanged phenol (28) remained and the product was shown by ^{1}H n.m.r. to consist of a mixture of the *cis*-(29) and *trans*-(30) dinitroketones, the 4-nitrodienone (55),[61] a compound assigned the 6-nitrodienone structure (56) and the 6-hydroxydienone (31)[40] (Refer Scheme 13). The evidence for the presence of the 6-nitrodienone (56) in the mixture was a ^{1}H n.m.r. signal at *c*.δ1.68 characteristic of the 6-methyl of 6-nitrodienones[38] (Refer Scheme 4). Because of the limited stability of the components of the mixture it was not possible to effect a separation.

Reaction of the 6-hydroxycyclohexa-2,5-dienone (31) in cyclohexane with nitrogen dioxide, reported earlier,[40] was repeated under conditions identical to those employed in the reaction of the phenol (28). The yields of the dinitroketones (29) and (30) (58%,42%) are in close agreement with those for the phenol (28) reaction indicating the probable intermediacy of the hydroxydienone (31) in the reaction pathway.

From the results of the short-term reaction it is clear that the 4-nitrodienone (55), the 6-nitrodienone (56) and the 6-hydroxydienone (31) are present during the conversion of phenol (28) into the dinitroketones (29) and (30). Hence, given the known addition of nitrogen dioxide to the 6-hydroxydienone (31), it seems probable on the basis of the evidence presented here that the formation of the dinitroketones (29) and (30) occurs as shown in Scheme 13. It appears, therefore, that the reactions of phenol (28) with the two reagent systems, fuming

nitric acid in acetic acid and nitrogen dioxide in cyclohexane, lead to essentially the same sequence of intermediates and product compositions.[60]

3.3.2 REACTION OF 2,4-DIBROMO-3,5,6-TRIMETHYLPHENOL WITH NITROGEN DIOXIDE

Reaction of 2,4-dibromo-3,5,6-trimethylphenol (57) (Refer Block F) in cyclohexane with nitrogen dioxide for 2h, as described in the general procedure, gave a precipitate (87%) which, after removal by filtration, was shown by infrared spectroscopy and elemental analysis to be a mixture of 2,5,6-trinitrocyclohex-3-enones (58). No hydroxyl group containing species were evident. The residue produced by evaporation of the solvent from the filtrate consisted of a complex mixture as indicated by ^{1}H n.m.r. and infrared spectroscopy. Because of the limited stability of the mixture of precipitated 2,5,6-trinitrocyclohex-3-enones (58) it was not possible to separate pure compounds. From the ^{1}H n.m.r. spectrum of the trinitroketone mixture (58) it was clear that the major trinitroketone isomer (58a) present was identical with a trinitroketone obtained during the nitration of phenol (57) with fuming nitric acid in acetic acid.[60] The remaining trinitroketone material (58b) was markedly unstable in polar solvents. On storage in deuteriochloroform solution the crude trinitroketone mixture was converted into a mixture of the *cis*-(59) and *trans*-(60) hydroxydinitroketones (the *trans*-epimer being present initially in greater than equilibrium quantity), which, after several days, yielded the α-diketone (61).[60] Similar rearrangement of the trinitroketone mixture was observed during storage in deuterioacetic acid solution.

Reaction of 2,4-dibromo-3,5,6-trimethylphenol (57) in acetic acid (instead of cyclohexane) with nitrogen dioxide for 8h, as described in the general procedure, gave, in contrast, a precipitate which was shown to be pure trinitroketone (58a) (44%). The residue obtained by evaporation of the solvent from the filtrate was shown by ^{1}H n.m.r. spectroscopy to consist of a mixture of the C2-epimeric hydroxydinitroketones (59) and (60) (each approximately 24% of the total reaction product), identical in all respects to the products obtained from the fuming nitric acid reaction of phenol (57) in acetic acid.[60] The absence of trinitroketone(s) (58b) from the products is completely in keeping with its known marked instability in acetic acid, as determined by a control experiment.[60]

On storage in deuteriochloroform solution the trinitroketone (58a) was relatively rapidly ($t_{\frac{1}{2}}$ *c.* 20 min) converted into a mixture of the *cis*-(59) and *trans*-(60) hydroxydinitroketones, the ratio being *c.* 4:5 at 70% conversion of the trinitroketone (58a) (30 min). Subsequently isomerisation of *trans*-(60) to *cis*-(59) hydroxydinitroketones occurred to give the equilibrium mixture (*c.* 2.5:1) of the *cis*-(59) and *trans*-(60) hydroxydinitroketones. Unfortunately, satisfactory crystals of trinitroketone (58a) could not be produced for X-ray crystallographic studies.

Comparison of the results of the nitration of 2,4-dibromo-3,5,6-trimethylphenol (57) with fuming nitric acid in acetic acid and nitrogen dioxide in cyclohexane[60] allows certain conclusions to be reached. From the reactions discussed above, it appears likely that both reagent systems convert the substrate phenol (57) into trinitroketones (58), but that the markedly less stable trinitroketone(s) (58b) is hydrolysed in acetic acid (with or without nitric acid being present) to give the

C2-epimeric hydroxydinitroketones (59) and (60). These results are in clear contrast to the patterns of reaction observed for the halogenated 6-methyl phenols considered previously (Section 3.3.1) which yield only 6-hydroxydinitroketones.[37,38,40,43] The crucial structural feature of phenol (57), in leading to the observed reaction pattern, is the C5-methyl group. Comparison of the structures, and results of nitration, of phenols (5) and (57) allows some comment to be made. These phenols differ only in the replacement of the C5-bromine in phenol (5) by a C5-methyl group in phenol (57). The overall reaction scheme for these phenols (5) and (57) is presented in Scheme 14. Two rationalisations of the observed results appear possible. First, and less likely, is that replacement of a C5-methyl group by a C5-bromine might accelerate the conversion of the 6-nitrodienone (C) into the 6-hydroxydienone (E) (*via* the 6-nitritodienone (D)). Second, and more likely, is that the inductively electron-donating C5-methyl group in phenol (57) may promote reaction of the 6-nitrodienone (C) with nitrogen dioxide to give the trinitroketones (F). In accord with this explanation, nitrogen dioxide is known[50,51,53] to be a free-radical with electrophilic character and attack on 2,4-dienes systems has been shown to proceed by nitrogen dioxide attack at carbon-5.[38,39,40]

Notwithstanding the above discussion, it is appreciated that hydroxydinitroketones have been isolated from nitric acid nitrations and nitrogen dioxide - acetic acid reactions of phenol (57). Although no definitive evidence is available, it appears likely that these hydroxydinitroketones arise by subsequent reaction of a first-formed trinitroketone mixture (58). In contrast for phenols (2), (5), (28) and (41), lacking

a C5-methyl group, no evidence has been obtained which points to formation of hydroxydinitroketones (10), (8), (29), (30), (42) and (43) by a route other than addition of nitrogen dioxide to the corresponding 6-hydroxydienones.

CHAPTER 4

NITRATION OF POLYALKYLATED PHENOLS WITH NITROGEN DIOXIDE

4.1 INTRODUCTION

The nitration of halogenated polysubstituted 6-methylphenols with nitrogen dioxide in organic solvents has been shown[60] to give 6-hydroxy-2,5-dinitrocyclohex-3-enones, which are identical with the products obtained from fuming nitric acid nitration of the corresponding phenols. A reaction scheme compatible with the experimental observations for the reactions of 6-methylphenols with nitrogen dioxide is presented in Scheme 14.

As was demonstrated in Chapter 3, the nature of the carbon-5 substituent has a pronounced effect on the distribution and type of products from the reactions of polyhalogenated phenols with nitrogen dioxide. For example, the replacement of the C5-bromine atom in phenol (5) with a methyl group to give phenol (57) changes the reaction products from, in the former case, a single 6-hydroxy-2,5-dinitrocyclohex-3-enone (10)[38] to, in the latter case, a mixture of two C2-epimeric 6-hydroxy-2,5-dinitrocyclohex-3-enones (59) and (60) plus two (or more) 2,5,6-trinitrocyclohex-3-enones (58).[60] This difference in product type and distribution, presumably due to the electronic effect of the carbon-5 substituent, renders the comparison of the reactions of halogenated phenols with nitrogen dioxide difficult. It would seem desirable to study the reactions, with nitrogen dioxide, of a series of phenols in which a substituent change does not alter the total electronic effect of the substituents to any great extent. An ideal choice for such a

study is represented by the 2,4,6-trialkylphenols in that the electronic effect of a substituent does not vary greatly with respect to the type and steric bulk of the substituent.

In contrast to the reactions of the halogenated phenols (Chapter 3), the nitration of 2,6-di-t-butyl-4-methylphenol (62) with nitrogen dioxide in light petroleum has been reported[56] to give a single product, the 6-hydroxy-4,5-dinitrocyclohex-2-enone (63), the stereochemistry of which was not determined. The mode of formation of the cyclohex-2-enone (63) was envisaged as occuring as shown in Scheme 15.[56] The presence of the phenoxy radical intermediate in the formation of the 4-nitrocyclohexa-2,5-dienone (64) was demonstrated by the detection and characterisation of its e.s.r. spectrum.[56] The formation of the intermediate 6-nitritoketone (65) from the intermediate radical in the penultimate step was attributed to steric hindrance by the 6-t-butyl group.

The general reaction procedure for the 2,4,6-trialkylphenols is identical to the procedure described for the halogenated 6-methylphenols (Chapter 3, Section 3.3), although in all cases the phenols themselves were soluble in the chosen solvents rather than being suspended solids.

4.2 DISCUSSION: REACTION OF 4-t-BUTYL-2,6-DIMETHYLPHENOL WITH NITROGEN DIOXIDE

Reaction of 4-t-butyl-2,6-dimethylphenol (66)[63a] with nitrogen dioxide in cyclohexane,[64] as for the general procedure described in Chapter 3, Section 3.3, for 2h gave a crude product from which the 6-hydroxy-2,4,5-trinitrocyclohex-3-enone (67) (Refer Block G) was obtained by crystallisation. This compound (67) is formed, along with its C2-epimer (68), in the reaction

of 2,6-dimethyl-4-nitrophenol (69) with either fuming nitric acid in acetic acid or nitrogen dioxide in cyclohexane.[62] The hydroxytrinitroketone (67), and presumably its C2-epimer (68) which was not isolated, are probably the result of nitrode-t-butylation of 4-t-butyl-2,6-dimethylphenol (66) to give the 4-nitrophenol (69), which then reacts with nitrogen dioxide in cyclohexane solution. Because of this complication, the separation of the products from the reaction of 4-t-butyl-2,6-dimethylphenol (66) with nitrogen dioxide in cyclohexane was not attempted. The ratio of products formed was estimated (See Reference 64) by comparison of ^{1}H n.m.r. spectra of the crude reaction mixture with those of ketones (67) and (68) and of the components separated, see below, from a reaction performed in benzene solution.

Reaction of 4-t-butyl-2,6-dimethylphenol (66) with nitrogen dioxide in benzene,[64] as for the general procedure in Chapter 3, Section 3.3, for 2h resulted in no detectable nitrode-t-butylation, but gave a crude product shown to be a mixture (*c.* 4:2:2:1:1 by ^{1}H n.m.r.) of the four isomeric trinitrocyclohex-3-enones (70), (71), (72) and (73) (Refer Block H) and the hydroxydinitro-cyclohex-3-enone (74). Separation of the crude mixture on a Chromatotron silica gel plate (suitably deactivated by repeated treatment with methanol) and subsequent recrystallisation of the isolated fractions provided pure crystalline samples of each of the five components (70)-(74).

In view of the fact that no 2,5,6-trinitrocyclohex-3-enones of sufficient stability had been isolated previously and also because the analysis of the spectroscopic data for the trinitroketones (70)-(73) did not allow unambiguous assignment of the stereochemistry of these compounds, it was deemed

necessary to establish the structures of at least three of the trinitroketones (70)-(73) by X-ray crystal structure analysis; the structure of the remaining trinitroketone would then be defined by exclusion. The trinitroketones chosen for X-ray crystal structure analysis were compounds (71),(72) and (73).[64] This choice was based upon consideration of both the chemical stability and crystal quality of the four compounds. Trinitroketone (70) decomposes more rapidly than the other trinitroketones and tends to form small, poorly developed crystals, rendering it unsuitable for X-ray structure analysis.

Similarly, analysis of the spectroscopic data for hydroxydinitroketone (74) did not allow unambiguous assignment of the hydroxyl group position or indeed of the relative stereochemistry of this compound, and it was deemed necessary to establish the structure by X-ray crystal structure analysis.[64]

Considering the 2,5,6-trinitrocyclohex-3-enones (71), (72) and (73), perspective drawings of 4-t-butyl-2,6-dimethyl-*r*-2, *c*-5,*t*-6-trinitrocyclohex-3-enone (71), 4-t-butyl-2,6-dimethyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (72) and 4-t-butyl-2,6-dimethyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (73) are presented in Figures 5, 6 and 7 respectively, with corresponding atomic coordinates in Tables 3, 4 and 5 respectively. The trinitroketones (71), (72) and (73) differ only in the relative orientations of the carbon-2, carbon-5 and carbon-6 substituents, the trinitroketone (71) having the *r*-2,*c*-5,*t*-6 trinitro stereochemistry, the trinitroketone (72) the *r*-2,*t*-5,*t*-6 trinitro stereochemistry and the trinitroketone (73) the *r*-2,*c*-5,*c*-6 trinitro stereochemistry. By exclusion, the trinitroketone (70) must contain the *r*-2,*t*-5,*c*-6 trinitro stereochemistry. In the solid state the ring conformations of the three trinitroketones

(71), (72) and (73) are similar, all existing in flattened skew-boat conformations as indicated by the relevant torsional angles: C(1)-C(2)-C(3)-C(4) 20.0(5)° and C(3)-C(4)-C(5)-C(6) -35.8(5)° for trinitroketone (71), C(1)-C(2)-C(3)-C(4) 6.7(5)° and C(3)-C(4)-C(5)-C(6) -35.7(5)° for trinitroketone (72) and C(1)-C(2)-C(3)-C(4) 11.6(4)° and C(3)-C(4)-C(5)-C(6) -38.4(4)° for trinitroketone (73), with the C5-nitro function in a "flagpole" orientation in all three of the compounds. For the trinitroketones (71) and (72), the C5-nitro function is disposed such that the C(5)-H(5) bond lies close to the plane of the nitro group (for compound (71) H(5)-C(5)-N(5)-O(52) 172(2)°, compound (72) H(5)-C(5)-N(5)-O(52) 173(2)°); in trinitroketone (73) the eclipsing is less exact, H(5)-C(5)-N(5)-O(52) -23°. It appears that the orientation of the C2-nitro function relative to the ring system is dependent on the relative stereochemistry of the C2 and C5-nitro functions. For trinitroketone (72) which has *trans*-2,5-dinitro stereochemistry, the C2-nitro function is close to eclipsed with the C(1)-C(2) bond, while in the *cis*-2,5-dinitro compounds (71) and (73) the C2-nitro functions are close to eclipsed with the C(2)-C(3) bond. Presumably, these stereochemical features extend to the trinitroketone (70), whose structure was not determined, given the spectroscopic similarity of the compound (70) with the trinitroketones (71), (72) and (73) (See Experimental).

For 6-hydroxy-2,5-dinitroketone (74) a perspective drawing of 4-t-butyl-*c*-6-hydroxy-2,6-dimethyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (74) is presented in Figure 8, with corresponding atomic coordinates in Table 6. The 6-hydroxydinitroketone (74) has an all-*cis* configuration of the C2-nitro, C5-nitro and C6-hydroxyl functions. In the solid state the ring conformation

is a flattened half-chair as indicated by the relevant torsion angles: C(1)-C(2)-C(3)-C(4) -3.0(6)^{o} and C(3)-C(4)-C(5)-C(6) -28.5(6)^{o}. The C5-nitro function has a pseudoaxial conformation as indicated by the torsional angle: C(3)-C(4)-C(5)-N(5) 90.1(4)^{o} and has an eclipsed orientation relative to H(5) as indicated by the torsional angle: H(5)-C(5)-N(5)-O(52) O(2)^{o}. In the crystalline state the C2-nitro function is orientated such that the N(2)-O(21) bond is close to eclipsed with the C(2)-C(3) bond, as indicated by the torsional angle: O(21)-N(2)-C(2)-C(3) 19.4(5)^{o}. For compound (74) there is evidence for intramolecular hydrogen bonding. In the structure (74), the O(1)-O(6) distance is 2.66Å, the HO(6)-O(1) distance is 2.23Å and the O(1)-C(1)-C(6)-O(6)-HO(6) system is somewhat out-of-plane (O(1)-C(1)-C(6)-O(6) 11.3(6)^{o}, C(1)-C(6)-O(6)-HO(6) 16(3)^{o}) indicating that the hydrogen bonding is probably weak. Computer generated packing plots of the crystal unit cell indicate the absence of an extended hydrogen bonding network in the crystal.

In all of the structures (71)-(74) the carbon-6 substituent occupying the position *trans*- to the C5-nitro function is in an *anti*-orientation with respect to this group as indicated by the relevant torsional angles: N(5)-C(5)-C(6)-N(6) 172.2(5)^{o} for trinitroketone (71), N(5)-C(5)-C(6)-C(9) 175.0(5)^{o} for trinitroketone (72), N(5)-C(5)-C(6)-C(9) 178.7(4) for trinitroketone (73) and N(5)-C(5)-C(6)-C(9) 168.0(6)^{o} for hydroxydinitroketone (74). Dreiding models of the compounds (70)-(74) indicate that it is probably the requirement of the C5-nitro function to occupy the "flagpole" position in compounds (70)-(73), or the pseudoaxial position in compound (74), that determines the alicyclic ring conformation and hence, as a corollary, forces the carbon-6 substituent *trans*- to the C5-nitro

function to occupy the corresponding *anti*-position. The preference of sterically demanding C5-substituents for the C5-axial orientation in cyclohexenones with skew-boat conformations has been recently demonstrated for the cyclohex-2-enone derivatives (75) and (76) (Refer Block I).[65]

Reaction of 4-t-butyl-2,6-dimethylphenol (66) with two molar-equivalents of nitrogen dioxide in benzene solution[64] gave a crude product, shown (by ^{1}H n.m.r. and infrared spectra) to consist largely of the 4-nitrocyclohexa-2,5-dienone (77) (Refer Block I). The purified 4-nitrodienone (77), obtained by separation of the crude mixture on a Chromatotron silica gel plate, was un unstable oil, but its spectroscopic characteristics (especially the infrared and ultraviolet absorption spectra which featured absorption bands characteristic of 2,5-dienones[66] and the simplicity of the ^{1}H n.m.r. spectrum which indicated a plane of symmetry in the molecule) were consistent with the assigned structure. However, the presence of small amounts of the isomeric 6-nitrocyclohexa-2,4-dienone (78) (Refer Block I) in the sample can not be excluded. A sample of the 4-nitrodienone (77), identical to that prepared above, was obtained from the reaction of phenol (66) with fuming nitric acid in acetic acid.[64]

Reaction of the 4-nitrodienone (77) with nitrogen dioxide in benzene, as for the reaction of the phenol (66) above, resulted in its complete conversion into a mixture of the four trinitroketones (70), (71), (72) and (73) and the 6-hydroxy-dinitroketone (74).[64] The ratio of products formed (*c.* 9:4:4:1:2 for (70):(71):(72):(73):(74), by ^{1}H n.m.r.) was similar to that found for the reaction of the phenol (66) with nitrogen dioxide in benzene, consistent with the intermediacy of the 4-nitrodienone (77) in the reaction pathway.

Control experiments were performed by treating, separately, the pure trinitroketones (70)-(73) in benzene with nitrogen dioxide. Essentially quantitative recovery of the pure isomer in all of the control experiments demonstrated that the trinitroketones (70)-(73) were not in equilibrium with one another under the reaction conditions. Additionally it was clear that the trinitroketone (73) is not converted, in the reaction system, into the hydroxydinitroketone (74); compound (74) is thus a primary reaction product. Similarly, long-term absorption of the trinitroketone (73) on the silica gel separating medium did not give rise to the formation of compound (74), removing the possibility that compound (74) is an artefact of the separatory technique.

4.3 DISCUSSION: REACTION OF 2-t-BUTYL-4,6-DIMETHYLPHENOL WITH NITROGEN DIOXIDE

Reaction of 2-t-butyl-4,6-dimethylphenol (79)[63b] with nitrogen dioxide in benzene, as for the general procedure in Chapter 3, Section 3.3, for 5h resulted in no detectable nitrode-t-butylation but gave a crude product shown to be a mixture (*c*. 1:1 by ^{1}H n.m.r.) of the two C4-epimeric 4,5,6-trinitrocyclohex-2-enones (80) and (81) (Refer Block J). Fractional crystallisation of the crude mixture from dichloromethane/pentane mixtures provided pure samples of both compounds (80) and (81). A first-order analysis of the spectroscopic data for the trinitroketones (80) and (81) did not allow unambiguous assignment of the stereochemistry of these compounds. Since there are four possible isomeric forms for the 4,5,6-trinitrocyclohex-2-enones arising from the reaction of phenol (79) with nitrogen dioxide, it was necessary

to establish the structure of both compounds (80) and (81) by X-ray crystal structure analysis.

A perspective drawing of 2-t-butyl-4,6-dimethyl-*r*-4,*c*-5,*t*-6-trinitrocyclohex-2-enone (80) is presented in Figure 9 with corresponding atomic coordinates in Table 7. Similarly, a perspective drawing of 2-t-butyl-4,6-dimethyl-*r*-4,*t*-5,*c*-6-trinitrocyclohex-2-enone (81) is presented in Figure 10 with corresponding atomic coordinates in Table 8. The trinitroketones (80) and (81) differ only in the relative positions of the C4-substituents. A *trans*- C5-nitro, C6-nitro configuration is adopted in both compounds, the less soluble isomer (80) having a *cis*- C4-nitro, C5-nitro configuration and the more soluble isomer (81) having a *trans*- C4-nitro, C5-nitro configuration. In the solid state the ring conformations of the two trinitroketones are dissimilar. The trinitroketone (80) exists in a flattened skew-boat conformation as indicated by the relevant torsional angles: C(6)-C(1)-C(2)-C(3) $-23(1)^{\circ}$ and C(2)-C(3)-C(4)-C(5) $4(1)^{\circ}$, with the C6-methyl group and the C5-hydrogen atom in "flagpole" orientations. In contrast, the trinitroketone (81) exists in a flattened half-chair conformation as indicated by the relevant torsional angles: C(6)-C(1)-C(2)-C(3) $-22(1)^{\circ}$ and C(2)-C(3)-C(4)-C(5) $-11(1)^{\circ}$, with the C6-methyl group in an axial and the C5-hydrogen atom in a pseudoaxial orientation. The olefinic and carbonyl functions in trinitroketones (80) and (81) are far from coplanar; for the trinitroketone (80) the O(1)-C(1)-C(2)-C(3) torsional angle is *c*. 161° whilst for trinitroketone (81) the corresponding angle is *c*. 164°. The existence of similar conformations in solution is supported by the ultraviolet absorption coefficients for compound (80) (ε 6100) and compound (81) (ε 5400), the low ε-values indicating non-planarity of the conjugated system for

both compounds.

Reaction of 2-t-butyl-4,6-dimethylphenol (79) with two molar-equivalents of nitrogen dioxide in benzene solution gave a crude product, shown (by ^{1}H n.m.r. and infrared spectra) to consist primarily of the 4-nitrocyclohexa-2,5-dienone (82) (Refer Block J). The pure 4-nitrodienone (82),[33] obtained by recrystallisation of the crude material from dry methanol, had spectroscopic properties entirely consistent with a cyclohexa-2,5-dienone structure.[66] A sample of the 4-nitrodienone (82), identical to that prepared above, was obtained from the reaction of phenol (79) with fuming nitric acid in acetic acid.[33] Although ^{1}H n.m.r. and ultraviolet spectroscopy studies of the pure 4-nitrodienone (82) provided no evidence for the existence of an equilibrium between the 4-nitrodienone (82) and the corresponding 6-nitrocyclohexa-2,4-dienone (83) (Block J), the presence of small amounts of the 6-nitrodienone (83) in the sample can not be excluded.

Reaction of the 4-nitrodienone (82) with nitrogen dioxide in benzene, as for the reaction of the phenol (79) above, resulted in its complete conversion into a mixture of the trinitroketones (80) and (81). The ratio of compound (80) to compound (81) (*c.* 1:1 by ^{1}H n.m.r.) being identical to that obtained for the reaction of the phenol (79) with nitrogen dioxide in benzene.

Control experiments were performed by treating, separately, the pure trinitroketones (80) and (81) in benzene with nitrogen dioxide. Essentially quantitative recovery of the pure isomer in either experiment demonstrated that the two trinitroketones (80) and (81) are not in equilibrium with one another under the reaction conditions.

4.4 DISCUSSION: REACTION OF 2,4-DI-t-BUTYL-6-METHYLPHENOL WITH NITROGEN DIOXIDE

Reaction of 2,4-di-t-butyl-6-methylphenol (84)[63c] with nitrogen dioxide in benzene, as for the general procedure in Chapter 3, Section 3.3, for 2h resulted in no detectable nitrode-t-butylation but gave a crude product shown to be a mixture (*c.* 39:30:14:3:7:4:3) of the four epimeric 2,5,6-trinitrocyclohex-3-enones (85), (86), (87) and (88) (Refer Block K), the two C6-epimeric 2-hydroxy-5,6-dinitrocyclohex-3-enones (89) and (90) and the 6-hydroxy-2,5-dinitrocyclohex-3-enone (91). Separation of the crude mixture on a Chromatotron silica gel plate (suitably deactivated by repeated treatments with methanol) and subsequent recrystallisation of the isolated fractions provided pure crystalline samples of each of the seven components (85)-(91).

First-order analysis of the spectroscopic data for the trinitroketones (85)-(88), first in isolation and then in comparison with the spectroscopic data for the trinitroketones (70)-(73) whose structure had been determined previously,[64] did not allow unambiguous assignment of the stereochemistry of these compounds. Thus it was necessary to establish the structures of at least three of the trinitroketones (85)-(88) by X-ray crystal structure analysis; the structure of the remaining trinitroketone would then be defined by exclusion. The trinitroketones chosen for X-ray crystal structure analysis were compounds (86), (87) and (88).

Similarly, analysis of the spectroscopic data for the hydroxydinitroketones (89), (90) and (91) did not allow unambiguous assignment of the hydroxyl group position or the relative stereochemistry in each compound so that it was

necessary to establish the structures of compounds (89), (90) and (91) by X-ray crystal structure analysis.

Considering firstly the 2,5,6-trinitrocyclohex-3-enones (86), (87) and (88), perspective drawings of 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*t*-6-trinitrocyclohex-3-enone (86), 2,4-di-t-butyl-6-methyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (87) and 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (88) are presented in Figures 11, 12 and 13 (molecules one and two in the crystallographic asymmetric unit of compound (87)), and 14 respectively, with corresponding atomic coordinates in Tables 9, 10 and 11, and 12 respectively. The trinitroketones (86), (87) and (88) differ only in the relative orientations of the carbon-2, carbon-5 and carbon-6 substituents, the trinitroketone (86) having the *r*-2,*c*-5,*t*-6 trinitro stereochemistry, the trinitroketone (87) the *r*-2,*t*-5,*t*-6 trinitro stereochemistry and the trinitroketone (88) the *r*-2,*c*-5,*c*-6 trinitro stereochemistry. By exclusion, the trinitroketone (85) must contain the *r*-2,*t*-5,*c*-6 trinitro stereochemistry. In the solid state the ring conformations of the three trinitroketones (86), (87) and (88) are quite different. Trinitroketones (86) and (88) exist in flattened skew-boat conformations as indicated by the relevant torsional angles: C(1)-C(2)-C(3)-C(4) 12.1(9)^{o} and C(3)-C(4)-C(5)-C(6) -31.1(8)^{o} for trinitroketone (86) and C(1)-C(2)-C(3)-C(4) 16.4(7)^{o} and C(3)-C(4)-C(5)-C(6) -39.4(5)^{o} for trinitroketone (88). In contrast, both of the chemically equivalent but crystallographically distinct molecules of trinitroketone (87) in the crystal asymmetric unit exist in flattened half-chair conformations as indicated by the relevant torsional angles: C(1)-C(2)-C(3)-C(4) -0.6(7)^{o} and C(3)-C(4)-C(5)-C(6) -30.1(6)^{o} for molecule one of trinitroketone (87) and

C(16)-C(17)-C(18)-C(19) -1.4(7)^{o} and C(18)-C(19)-C(20)-C(21) -25.2(6)^{o} for molecule two of trinitroketone (87). In all three of the trinitroketones (86)-(88), the C5-nitro function is disposed such that the C(5)-H(5) bond lies close to the plane of the nitro group (for compound (86) H(5)-C(5)-N(5)-O(52) -2(3)^{o}, compound (87) H(5)-C(5)-N(5)-O(52) -7(3)^{o} for molecule one and H(20)-C(20)-N(5')-O(52') -19(3)^{o} for molecule two, compound (88) H(5)-C(5)-N(5)-O(52) -14(2)^{o}). Unlike trinitroketones (71)-(73) (Section 4.2) where the orientation of the C2-nitro function relative to the ring system is dependent on the relative stereochemistries of the C2 and C5-nitro functions, the orientation of the C2-nitro function in trinitroketones (86)-(88) appears to be determined by the presence of the C2-t-butyl group. In all three trinitroketones (86)-(88), the C2-nitro function is disposed such that the C(2)-C(2)-t-butyl group bond lies at approximately right-angles to the plane of the nitro group (for compound (86) C(7)-C(2)-N(2)-O(21) 100.6(6)^{o}, compound (87) C(7)-C(2)-N(2)-O(21) -83.8(5)^{o} for molecule one and C(22)-C(17)-N(2')-O(21') 91.3(5)^{o} for molecule two, compound (88) C(7)-C(2)-N(2)-O(21) 99.9(4)^{o}). This interaction between the C2-t-butyl group and the C2-nitro function is also evident in the notable lengthening of the C(2)-C(2)-t-butyl bond in compounds (86)-(88) (compound (86) C(2)-C(7) 1.605(8)$\mathring{A}$, compound (87) C(2)-C(7) 1.581(6)$\mathring{A}$ for molecule one and C(17)-C(22) 1.570(6)$\mathring{A}$ for molecule two, compound (88) C(2)-C(7) 1.590(6)$\mathring{A}$; compared to the average C-C bond length of 1.52-1.56$\mathring{A}$). Presumably, these stereochemical features extend to the trinitroketone (85), whose structure was not determined, given the spectroscopic similarity of compound (85) with the trinitroketones (86), (87) and (88) (See Experimental).

For the two C6-epimeric hydroxydinitroketones (89) and (90), perspective drawings of 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*c*-6-dinitrocyclohex-3-enone (89) and 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*t*-6-dinitrocyclohex-3-enone (90) are presented in Figures 15 and 16, respectively with corresponding atomic coordinates in Tables 13 and 14, respectively. The hydroxydinitroketones (89) and (90) differ only in the relative orientation of the carbon-6 substituents, the hydroxydinitroketone (89) having the *r*-2-hydroxy,*t*-5,*c*-6 dinitro stereochemistry whilst the hydroxydinitroketone (90) has the *r*-2-hydroxy,*t*-5,*t*-6 dinitro stereochemistry. In the solid state the ring conformations for compounds (89) and (90) are dissimilar, hydroxydinitroketone (89) existing in a flattened half-chair conformation as indicated by the relevant torsional angles: C(1)-C(2)-C(3)-C(4) $-3.3(6)^{\circ}$ and C(3)-C(4)-C(5)-C(6) $-21.8(5)^{\circ}$ while hydroxydinitroketone (90) exists in a flattened skew-boat conformation as indicated by the relevant torsional angles : C(1)-C(2)-C(3)-C(4) $2.3(6)^{\circ}$ and C(3)-C(4)-C(5)-C(6) $-29.2(5)^{\circ}$. The C5-nitro functions in compounds (89) and (90) are in pseudoaxial and "flagpole" orientations respectively as indicated by the torsional angles: C(3)-C(4)-C(5)-N(5) $97.2(4)^{\circ}$ for compound (89) and $92.9(4)^{\circ}$ for compound (90) and have eclipsed orientations relative to their C5-hydrogen atoms as indicated by the torsional angles: H(5)-C(5)-N(5)-O(52) $11(2)^{\circ}$ for compound (89) and $165(2)^{\circ}$ for compound (90). For the hydroxydinitroketones (89) and (90) the C(2)-C(2)-t-butyl group bond lengths, unlike the corresponding bond lengths in the trinitroketones (86)-(88) which are unusually lengthened, are within the range normally expected for carbon-carbon single bonds (compound (89) 1.550(6)Å, compound (90) 1.565(6)Å).

Presumably, this shortening of the C(2)-C(2)-t-butyl bond length in compounds (89) and (90) is due to a reduced steric interaction between the C2-t-butyl group and a hydroxyl function as compared with the greater interaction between the C2-t-butyl group and the sterically much larger nitro function in trinitroketones (86)-(88). For compounds (89) and (90) there is a distinct lack of evidence for hydrogen bonding, intra- or intermolecular, involving the C2-hydroxyl function. In structure (90), the HO(2)-O(1) distance is 2.89Å; too long for an intramolecular hydrogen bond and no intermolecular distance from HO(2) is less than 3.5Å. Similarly, in structure (89) there are no intra- or intermolecular distances less than 3.5Å from HO(2). The absence of any extended weak hydrogen bonding in the crystalline state was confirmed by computer generated packing plots of the crystal unit cells for compounds (89) and (90).

For the 6-hydroxydinitroketone (91), a perspective drawing of 2,4-di-t-butyl-*c*-6-hydroxyl-6-methyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (91) is presented in Figure 17 with corresponding atomic coordinates in Table 15. The 6-hydroxy-2,5-dinitroketone (91) has an all-*cis* configuration of the C2-nitro, C5-nitro and C6-hydroxyl functions. In the solid state the ring conformation for compound (91) is a flattened skew-boat as indicated by the relevant torsional angles: C(1)-C(2)-C(3)-C(4) 13.4(5)° and C(3)-C(4)-C(5)-C(6) -36.3(4)°. Once again, the C5-nitro function is in a "flagpole" orientation as indicated by the torsional angle: C(3)-C(4)-C(5)-N(5) 83.7(4)° and is disposed such that the C(5)-H(5) bond lies close to the plane of the nitro function (H(5)-C(5)-N(5)-O(52) -12(2)°). As in the trinitroketones (86)-(88), the C(2)-C(2)-t-butyl bond length

in compound (91) is lengthened, C(2)-C(7) 1.576(5)Å, compared to the C(2)-C(2)-methyl bond length in 6-hydroxydinitroketone (74), C(2)-C(7) 1.534(6)Å. Again, this interaction between the C2-t-butyl group and the C2-nitro function is also evident in that the C2-nitro function is disposed such that the C(2)-C(7) bond lies at approximately right-angles to the plane of the nitro function (C(7)-C(2)-N(2)-O(21) 95.3(3)^{o}). For compound (91) there is evidence for intramolecular hydrogen bonding. In the structure (91), the O(1)-O(6) distance is 2.64Å, the HO(6)-O(1) distance is 2.13Å and the O(1)-C(1)-C(6)-O(6)-HO(6) system is almost planar (O(1)-C(1)-C(6)-O(6) 25.9(4)^{0}, C(1)-C(6)-O(6)-HO(6) -22(2)^{o}) indicating intramolecular hydrogen bonding. Computer generated packing plots of the crystal unit cell indicate the absence of an extended hydrogen bonding network in the crystal.

Reaction of 2,4-di-t-butyl-6-methylphenol (84) with two molar-equivalents of nitrogen dioxide in benzene solution gave a crude product, shown (by ^{1}H n.m.r. and infrared spectra) to consist largely of the 4-nitrocyclohexa-2,5-dienone (92)[33] (Refer Block L). The purified 4-nitrodienone (92), obtained by separation of the crude mixture on a Chromatotron silica gel plate, was a pale-yellow crystalline material. Its spectroscopic characteristics, especially the characteristic infrared and ultraviolet absorption spectra,[66] were entirely consistent with the assigned structure (92). Although it could not be detected by ^{1}H n.m.r. spectroscopy, the presence of small amounts of the isomeric 6-nitrocyclohexa-2,4-dienone (93) (Refer Block L) in solutions of the 4-nitrodienone (92) can not be excluded. A sample of the 4-nitrodienone (92),

identical with that prepared above, was obtained from the reaction of phenol (84) with fuming nitric acid in acetic acid.[33]

Reaction of the 4-nitrodienone (92) with nitrogen dioxide in benzene, as for the reaction of the phenol (84) above, resulted in its complete conversion into a mixture of the four trinitroketones (85), (86), (87) and (88), the two C6-epimeric 2-hydroxydinitroketones (89) and (90) and the 6-hydroxydinitroketone (91). The ratio of products formed (*c.* 44:30:8:3:8:4:3 for (85):(86):(87):(88):(89):(90):(91)) was similar to that found for the reaction of the phenol (84) with nitrogen dioxide in benzene, consistent with the intermediacy of the 4-nitrodienone (92) in the reaction pathway.

Control experiments involving long-term absorption of trinitroketones (85), (87) and (88) on the silica gel separating medium did not give rise to the formation of the corresponding hydroxydinitroketones (89), (90) and (91). In addition to the fact that compounds (89), (90) and (91) can be detected, by ^{1}H n.m.r., in the crude product mixture from the reaction of phenol (84) with nitrogen dioxide, the above observation demonstrates that compounds (89), (90) and (91) are primary reaction products.

4.5 DISCUSSION: REACTION OF 2,6-DI-t-BUTYL-4-METHYLPHENOL WITH NITROGEN DIOXIDE

Reaction of 2,6-di-t-butyl-4-methylphenol (62) with nitrogen dioxide in cyclohexane,[67] as for the general procedure in Chapter 3, Section 3.3, but for only 10 min, gave an essentially quantitative yield of 2,6-di-t-butyl-4-methyl-4-nitrocyclohexa-2,5-dienone (64), identical in all respects with an authentic sample prepared by fuming nitric acid

nitration of the phenol (62),[33] as had been reported for the reaction of the phenol (62) with nitrogen dioxide in light petroleum.[56] The compound (64) (Refer Block M) was identified as the 4-nitrodienone (64) rather than the alternative 6-nitrodienone by its relatively simple ^{1}H n.m.r. spectrum which indicated a plane of symmetry in the molecule. In addition, the infrared and ultraviolet absorption spectra were characteristic of cyclohexa-2,5-dienones.[66]

Studies of a deuteriochloroform solution of 4-nitrodienone (64) by ^{1}H n.m.r. gave no evidence of a corresponding 6-nitrocyclohexa-2,4-dienone species, although a slow transformation proceeded eventually yielding the 4-hydroxycyclohexa-2,5-dienone (94).[67] Treatment of the 4-nitrodienone (64) with an acetic acid/sodium acetate buffer solution (Refer Experimental) afforded an authentic sample of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (94)[68] identical to the material obtained from the treatment of compound (64) with deuteriochloroform.

Extension of the reaction time to 22h for the reaction of phenol (62) with nitrogen dioxide in cyclohexane resulted in the partial conversion (See Experimental) of the initially formed 4-nitrodienone (64) into a mixture (*c.* 1:1 by ^{1}H n.m.r.) of the trinitrocyclohex-2-enone (95) and the hydroxydinitrocyclohex-2-enone (96)[67] (Refer Block M). A similar 22h treatment, under identical conditions in cyclohexane, of the 4-nitrodienone (64) with nitrogen dioxide provided a mixture of compounds (95) and (96) in almost identical yield and product ratio to the reaction of the phenol (62) with nitrogen dioxide.[67]

The markedly more labile 2,6-di-t-butyl-4-methyl-*r*-4,*c*-5,

c-6-trinitrocyclohex-2-enone (95) was isolated from the product mixture by crystallisation and its structure was established by X-ray crystal structure analysis.[67] A perspective drawing of the structure (95) is presented in Figure 18 with corresponding atomic coordinates in Table 16. The spectroscopic data (See Experimental) for compound (95) are in accord with its established structure.

The mother liquor from the above crystallisation was evaporated under reduced pressure to give a residue which was dissolved in chloroform/acetonitrile and stored at 20^{o} for 16h; during this treatment any residual trinitroketone (95) is converted into the more soluble 4-nitrodienone (64) by loss of nitrogen dioxide, a process demonstrated to occur in a control experiment on the pure trinitroketone (95).[67] Crystallisation of the residue from this treatment gave 2,6-di-t-butyl-*c*-6-hydroxy-4-methyl-*r*-4,*c*-5-dinitrocyclohex-2-enone (96), identical in all respects with the material (63) isolated by Brunton *et.al.*.[56] The stereochemistry of the 6-hydroxy-4,5-dinitroketone (96) was determined by X-ray crystal structure analysis.[67] A perspective drawing of the structure (96) is presented in Figure 19, with corresponding atomic coordinates in Table 17. The spectroscopic data (See Experimental) for compound (96) are in accord with its established structure.

The trinitroketone (95) and the hydroxydinitroketone (96) differ only in the nature of the C6-substituent; nitro or hydroxyl respectively. In the solid state the ring conformations of the two compounds are similar, both existing in a boat form as indicated by the relevant torsional angles: C(6)-C(1)-C(2)-C(3) -31(1)^{o} and C(2)-C(3)-C(4)-C(5) 38(1)^{o} for trinitroketone (95) and C(6)-C(1)-C(2)-C(3) -40(1)^{o} and C(2)-C(3)-C(4)-C(5) 42(1)^{o}

for hydroxydinitroketone (96), with the C4-nitro function in a "flagpole" orientation in both compounds. In neither structure are the olefinic and carbonyl functions coplanar; for the trinitroketone (95) the torsional angle O(1)-C(1)-C(2)-C(3) is *c.* 150° whilst for the hydroxydinitroketone (96) the corresponding angle is *c.* 141°. The existence of similar conformations in solution is supported by the ultraviolet absorption coefficients for compound (95) (ε 9700) and compound (96) (ε 4800) the larger ε-value for compound (95) indicating that the olefinic-carbonyl system is more nearly planar (although still considerably out-of-plane) in this compound than in compound (96).

Several control experiments were necessary to demonstrate the origin of compound (96). Firstly, trinitroketone (95) treated with nitrogen dioxide in cyclohexane gave an essentially quantitative recovery of compound (95), demonstrating that trinitroketone (95) is not in equilibrium with hydroxydinitroketone (96) under the reaction conditions. Similarly, treatment of a solution of trinitroketone (95) in dichloromethane with water gave quantitative recovery of compound (95), demonstrating that hydroxydinitroketone (96) is not a hydrolysis product of compound (95). 2,6-di-t-butyl-6-hydroxy-4-methylcyclohexa-2,4-dienone (97), generated by gentle heating of a chloroform solution of the hydroxydinitroketone (96), underwent addition of nitrogen dioxide in cyclohexane to give a complex mixture of products,[67] none of which appeared to correspond (^{1}H n.m.r.) to the hydroxydinitroketone (96). This result indicated that the compound (96) is not produced by the addition of nitrogen dioxide to the 6-hydroxydienone (97).

In benzene solution, reaction of the phenol (62) with nitrogen dioxide for 16h, as for the general procedure in

Chapter 3, Section 3.3, gave only the trinitroketone (95) in addition to the 4-nitrodienone (64); only minute traces of the hydroxydinitroketone (96) could be detected amongst the products.[67] This difference in reaction behaviour in cyclohexane and benzene solutions extended to the reaction of the 4-nitrodienone (64) with nitrogen dioxide, trinitroketone (95) alone being produced from the reaction in benzene solution.

4.6 DISCUSSION: REACTION OF 2,4,6-TRI-t-BUTYLPHENOL WITH NITROGEN DIOXIDE

Nitration of 2,4,6-tri-t-butylphenol (98) with fuming nitric acid in acetic acid had been reported previously[33,55] to give 2,4,6-tri-t-butyl-4-nitrocyclohexa-2,5-dienone (99) (Refer Block N). The same 4-nitrodienone (99) had also been produced by reaction of the 2,4,6-tri-t-butylphenoxy radical with nitrogen dioxide.[55]

Reaction of 2,4,6-tri-t-butylphenol (98) with nitrogen dioxide in cyclohexane, as for the general procedure in Chapter 3, Section 3.3, for 2 hr gave a quantitative yield of the 4-nitrodienone (99), identical in all respects with an authentic sample.[33,55] The spectroscopic data for compound (99) are consistent with the cyclohexa-2,5-dienone structure.

Similar reaction of 2,4,6-tri-t-butylphenol (98) in benzene, under identical conditions to the reaction in cyclohexane, with nitrogen dioxide for 2h again gave a quantitative yield of the 4-nitrodienone (99).

Extending the reaction time of the phenol (98) with nitrogen dioxide, in either cyclohexane or benzene, to 23h gave a mixture (*c.* 1:8:1 by ^{1}H n.m.r.) of the 4-nitrodienone (99),[33,55] 2,6-di-t-butylbenzo-1,4-quinone (100)[69] and

2-t-butyl-4,6-dinitrophenol (101)[70] (Refer Block N). A similar product mixture was obtained in an identical reaction with nitrogen dioxide of the 4-nitrodienone (99). Separation of the crude reaction product on a Chromatotron silica gel plate gave pure samples of each of the three compounds (99)-(101) (See Experimental).

A control experiment was performed to follow, by ^{1}H n.m.r., the decomposition of the 4-nitrodienone (99) in deuteriobenzene. The decomposition of compound (99) was complete in *c*. 24h at 30° and gave rise to a complex mixture; however the quinone (100) and the dinitrophenol (101) were not detected in the crude product mixture.

It seems likely that dinitrophenol (101) arises *via* de-t-butylation of the 4-nitrodienone (99) to give 2,6-di-t-butyl-4-nitrophenol (102) followed by subsequent nitration of the nitrophenol (102) by nitrogen dioxide. Addition of nitrogen dioxide to nitrophenol (102), under identical conditions to the reaction of phenol (98) above, gave a particularly unstable product which decomposed rapidly, even at 0°, to yield the dinitrophenol (101). The likely precursor to the dinitrophenol (101) in the above reactions is the 6-nitrocyclohexa-2,4-dienone (103). This compound had been suggested previously,[70b] on the basis of spectroscopic evidence, as an intermediate in the nitration of nitrophenol (102) with fuming nitric acid in acetic acid to give dinitrophenol (101).

4.7 DISCUSSION: REACTION PATHWAYS FOR THE REACTIONS OF 2,4,6-TRIALKYLPHENOLS WITH NITROGEN DIOXIDE

On the basis of the evidence presented in Sections 4.2-4.6 it is clear that for the nitration of any 2,4,6-trialkylphenol

with nitrogen dioxide in benzene the reaction processes illustrated in Scheme 16 are possible. In the discussion which follows, aspects of the reaction scheme will be highlighted and wherever possible the factors which determine the reaction fate of any intermediate will be identified.

4.7.1 NITRODIENONE FORMATION

It has been established previously, by other workers,[55,56] that conversion of 2,4,6-trialkylphenols (A) into nitrocyclohexadienones by nitrogen dioxide occurs *via* the interaction of the corresponding phenoxy radical and a nitrogen dioxide radical. The information available points to the formation, at least initially, of the 4-nitrocyclohexa-2,5-dienone (B) in each of the reactions. The position is less clear in relation to the mode of formation of the 6-nitrocyclohexa-2,4-dienones (C). Indeed, it is uncertain in the substrates considered in this Chapter whether the 6-nitrocyclohexa-2,4-dienones (C) are formed directly from combination of the corresponding phenoxy radical with nitrogen dioxide radical or whether they arise from the phenoxy radical, nitrogen dioxide radical-pair formed from the corresponding 4-nitrocyclohexa-2,5-dienone (B).

4.7.2 REACTION AS 4-NITROCYCLOHEXA-2,5-DIENONES OR 6-NITROCYCLOHEXA-2,4-DIENONES?

On the assumption that the 4-nitrocyclohexa-2,5-dienone (B) is the intermediate in the reaction sequence certain comments can be made. It is clear that rearrangement of the 4-nitrocyclohexa-2,5-dienone (B) to give the 6-nitrocyclohexa-2,4-dienone (C) occurs only in the situation where R_1 or R_3 = methyl. For compounds

where R_1=R_3=t-butyl, rearrangement of the 4-nitrodienone (B) to give the 6-nitrodienone (C) is blocked, and any reaction with nitrogen dioxide that does occur will involve the slow addition of nitrogen dioxide to the 4-nitrocyclohexa-2,5-dienone (B). To illustrate this point the 4-nitrodienone (64), derived from 2,6-di-t-butyl-4-methylphenol (62), forms the 4,5,6-trinitrocyclohex-2-enone (95) (Structure (D), Scheme 16) slowly and incompletely; indeed, trinitroketone (95) is in equilibrium with the 4-nitrodienone (64) under the reaction conditions.[67] In this case, initial attack by nitrogen dioxide on the 4-nitrodienone (64) occurs at a site (carbon-5) flanked by the C4-methyl group and the C6-t-butyl group. It is clear that for the 4-nitrodienone (99), derived from 2,4,6-tri-t-butylphenol (98), this attack at carbon-5 is impossible because of the combined steric effects of the C4 and C6-t-butyl groups.

4.7.3 STERIC EFFECTS IN THE REACTIONS OF 6-NITRODIENONES WITH NITROGEN DIOXIDE

Assuming that either R_1 or R_3 = methyl, rearrangement of the 4-nitrodienone (B) will give the 6-nitrodienone (C). There are two possible reaction fates for the 6-nitrodienone (C). Firstly, the 6-nitrodienone (C) can add nitrogen dioxide to the diene system to give trinitroketones ((G) or (H)), *via* the intermediate delocalised radical (E). Alternatively, the 6-nitrodienone (C) can undergo nitro-nitrito rearrangement followed by hydrolysis to give the 6-hydroxydienone (J), which will then undergo nitrogen dioxide addition to the diene system to give the 6-hydroxy-2,5-dinitroketones (K). Assuming that the C6-substituent remains constant, that is, R_3 = methyl, it

is likely that the rate of nitro-nitrito rearrangement of the 6-nitrodienone (C) will be essentially independent of the nature of the alkyl groups at C2 and C4. In contrast, the rate of addition of nitrogen dioxide to the 6-nitrodienone (C), initiated by nitrogen dioxide attack at C5, would be expected to reflect variations in the steric hindrance to attack at that position. In illustration, when R_2 = methyl (2-t-butyl-4,6-dimethylphenol (79)), reaction of the 6-nitrodienone (C) with nitrogen dioxide occurs rapidly, giving only the trinitroketones (G) (compounds (80) and (81)), derived from the intermediate delocalised radical (E). Formation of the 6-hydroxydienone (J) does not occur (as indicated by the absence of 6-hydroxy-2,5-dinitroketones (K) from the reaction of phenol (79) with nitrogen dioxide). However, when R_2 = t-butyl attack of the electrophilic nitrogen dioxide radical at carbon-5 in the 6-nitrodienone (C) will be hindered by the steric interaction between the incoming nitrogen dioxide radical and the C4-t-butyl group. The rate of addition of nitrogen dioxide to the 6-nitrodienone (C) will therefore be reduced. Under these circumstances the reaction pathway involving nitro-nitrito rearrangement becomes competitive, 6-hydroxydienones (J) are formed, and 6-hydroxy-2,5-dinitroketones (K) are isolated. For example, reaction of 4-t-butyl-2,6-dimethylphenol (66) with nitrogen dioxide in benzene gives the 2,5,6-trinitroketones (70), (71), (72) and (73) (90%) and the 6-hydroxy-2,5-dinitroketone (74) (10%).[64] Reaction of the structurally similar 2,4-di-t-butyl-6-methylphenol (84) with nitrogen dioxide in benzene gives the 2,5,6-trinitroketones (85), (86), (87) and (88) (86%) and the 6-hydroxy-2,5-dinitroketone (91) (3%).

4.7.4 STEREOCHEMISTRY OF NITROGEN DIOXIDE ATTACK ON CYCLOHEXA-2,4-DIENONES

The mode of reaction of the 6-hydroxycyclohexa-2,4-dienones (104) and (105), derived from the 6-nitrocyclohexa-2,4-dienones (78) and (93) respectively, with nitrogen dioxide is shown in Scheme 17. The conformation of a 6-hydroxydienone, as discussed previously (Introduction; Chapter 1) and as illustrated in Scheme 17, is determined by the strong intramolecular hydrogen bonding between the carbonyl and hydroxyl functions. In this conformation the C6-methyl group is held in such a position that it effectively shields the lower face of the diene system. Attack on the diene system at carbon-5 by nitrogen dioxide radical, the initiating step in the formation of the 6-hydroxy-2,5-dinitrocyclohex-3-enones, can thus occur only from the direction *cis*- to the C6-hydroxyl group. The delocalised radical intermediate thus formed is open to attack at carbon-2 by another nitrogen dioxide radical, although the direction of attack is now much less specific because of the absence of steric hindrance by the C6-methyl group. The result of this attack by nitrogen dioxide is the formation of both the *cis*- and the *trans*- 2,5-dinitro stereochemistry in the 6-hydroxy-2,5-dinitrocyclohex-3-enone ((K), Scheme 16) products. However, in the reactions of phenols (66) and (84) with nitrogen dioxide in benzene only the products with the *cis*-2,5-dinitro stereochemistry (compounds (74) and (91) respectively) could be isolated.

In the case of the 6-nitrocyclohexa-2,4-dienones ((C), Scheme 16), the stereoselectivity of nitrogen dioxide radical attack at carbon-5 is variable and also highly dependent on the nature of the alicyclic ring substituent R_2. For example,

addition of nitrogen dioxide at carbon-5 of the 6-nitrodienone (83), arising from 2-t-butyl-4,6-dimethylphenol (79) (R_2=methyl), occurs exclusively in a direction *trans*- to the C6-nitro function. The suggested mode of reaction of 6-nitrodienone (83) with nitrogen dioxide is illustrated in Scheme 18. If the 6-nitrodienone (83) exists in the conformation shown in Scheme 18, the C6-nitro function occupies a pseudoaxial position. As was observed for the axial C6-methyl group in the 6-hydroxydienones discussed above, the C6-nitro function effectively blocks the lower face of the diene system. Attack of the diene system at carbon-5 by nitrogen dioxide can thus only occur from the direction *trans*- to the C6-nitro function. The delocalised radical intermediate (compound (106)) thus formed is then attacked at carbon-4 by another nitrogen dioxide radical (See Section 4.7.5) to give the two C4-epimeric 4,5,6-trinitrocyclohex-2-enones (80) and (81).

When R_2 = t-butyl, as in the case for the 6-nitrodienones (78) and (93), arising from the phenols (66) and (84) respectively, addition of nitrogen dioxide at carbon-5 is observed to occur predominantly in a direction *trans*- to the C6-nitro function; however some addition is observed to occur such as to give *cis*-5,6-dinitro functions. The observed ratio of *trans:cis* addition of the C5-nitro (relative to the C6-nitro function) is similar for the two 6-nitrodienones (78) and (93) [for 6-nitrodienone (78), *trans*-5,6-dinitro products (70) + (71) = 60%, *cis*-5,6-dinitro products (72) + (73) = 30%; for 6-nitrodienone (93), *trans*-5,6-dinitro products (85) + (86) + (89) = 69%, *cis*-5,6-dinitro products (87) + (88) + (90) = 28%].

Two possible rationalisations can be envisaged for the ratio of *trans:cis* attack of nitrogen dioxide at carbon-5 in these

6-nitrodienones. First, the 6-nitrodienones (78) and (93) may exist and/or react in two different conformations, (*I*) and (*II*), as shown in Scheme 19. Attack by nitrogen dioxide at carbon-5 in conformation (*I*), where the C6-nitro function is in a pseudoaxial orientation, will result in the generation of a delocalised radical intermediate containing a *trans*-C5-nitro, C6-nitro structural feature (radicals (107a) and (108a) from 6-nitrodienone conformations (78a) and (93a) respectively). Similarly, attack by nitrogen dioxide at carbon-5 in conformation (*II*), where the C6-methyl group is pseudoaxial, will result in the generation of a delocalised radical intermediate containing a *cis*-C5-nitro, C6-nitro structural feature (radicals (107b) and (108b) from 6-nitrodienone conformations (78b) and (93b) respectively).

Second, it is possible that the 6-nitrodienones (78) and (93) both exist and react in conformation (*I*) (Scheme 20), but that in the presence of the bulky C4-t-butyl group the stereoselectivity induced by the orientation of the C6-nitro function is reduced. No information is available which would allow a distinction to be made between these two proposals.

4.7.5 REACTIONS OF DELOCALISED RADICAL (E)

In the reactions of the delocalised radical (E) (Scheme 16) with nitrogen dioxide a number of possibilities are open. Considering first the reaction of delocalised radical (E) with nitrogen dioxide ($\dot{N}O_2$), reaction may occur either at carbon-2 or carbon-4. For example, reaction of the delocalised radical (106) (Refer Scheme 18), derived from the 6-nitrodienone (83), with nitrogen dioxide ($\dot{N}O_2$) occurs exclusively at carbon-4, presumably due to the greater steric hindrance to attack at the

t-butyl substituted carbon-2.

For the delocalised radical (107), derived from the 6-nitrodienone (78), reaction with nitrogen dioxide ($\dot{N}O_2$) occurs exclusively at carbon-2, again a result of the differing steric compression at C2 and C4. For the delocalised radical (108), derived from the 6-nitrodienone (93), in which the steric effects at C2 and C4 would be expected, at first sight, to be similar, reaction occurs exclusively at carbon-2. This regioselectivity presumably arises because of the developing *gauche* interactions (C4-C5-C6) being experienced even at the transition-state for the alternative reaction, formation of 4,5,6-trinitrocyclohex-2-enones [(G), (Scheme 16)] by reaction of nitrogen dioxide ($\dot{N}O_2$) at carbon-4.

As to the formation of the 2-hydroxy-5,6-dinitrocyclohex-3-enones (89) and (90) from the delocalised radical (108), only limited information is available. It seems likely that these compounds arise by attack of the oxygen centre of nitrogen dioxide ($\dot{O}NO$) at carbon-2 of the delocalised radical (108) and that the initially-formed nitrito compound is hydrolysed to the 2-hydroxy compound either during the reaction or during the workup and isolation procedure. It is interesting to note that in the present work 2-hydroxy-5,6-dinitrocyclohex-3-enones [(I), (Scheme 16)] are only isolated in the reaction of the delocalised radical (108), derived from the 6-nitrodienone (93); in this case it may be significant that attack must occur at carbon-2 because of the presence of a C4-t-butyl group, but that reaction at carbon-2 encounters steric compression from the C2-t-butyl group. In these circumstances it is possible that nitrogen dioxide ($\dot{O}NO$) attack occurs because of the lower steric demand of this attacking species.

CHAPTER 5

FORMATION OF A HYDROXYNITROPHENOXYKETONE FROM 4-t-BUTYL-2,6-DIMETHYLPHENOL

During the study of the reaction of 4-t-butyl-2,6-dimethylphenol (66) with nitrogen dioxide in benzene (Section 4.2), the 4-nitrodienone (77) was required.[64] In the event it was found that reaction of the phenol (66) with limited amounts of nitrogen dioxide in benzene gave the 4-nitrodienone (77) in high yield. Early in the preliminary explorations utilising this synthetic method, the substituted hydroxynitrophenoxyketone (109) (Refer Block O) was isolated.[71]

Slow addition of a solution of nitrogen dioxide (1 mole-equivalent) in benzene to a solution of 4-t-butyl-2,6-dimethylphenol (66) in benzene gave a mixture from which the benzene solvent was removed at 20^{o} under reduced pressure. Addition of pentane to the oily residue caused the hydroxynitrophenoxyketone (109)[71] to precipitate out from the mixture (overall yield *c.* 26%, by weight). The mother liquor from this crystallisation was shown (by ^{1}H n.m.r.) to contain further ketone (109) (*c.* 10%) but no further components could be isolated from this unstable mixture.

The structure of compound (109) was established by X-ray crystal structure analysis.[71] A perspective drawing of this structure (109) is presented in Figure 20 with corresponding atomic coordinates in Table 18. The spectroscopic data for compound (109) are in accord with its established structure.

In the solid state the alicyclic ring conformation is a flattened half-chair as indicated by the torsional angles: C(1)-C(2)-C(3)-C(4) $-2.9(6)^{o}$ and C(3)-C(4)-C(5)-C(6) $-29.6(5)^{o}$. The C5-nitro function has a pseudoaxial conformation as indicated by the relevant torsional angle: C(3)-C(4)-C(5)-N(5) $89.4(4)^{o}$ and has the eclipsed orientation relative to the C(5)-H(5) bond as indicated by the relevant torsional angle: H(5)-C(5)-N(5)-O(52) $O(2)^{o}$. Similar conformations for the alicyclic ring and C5-nitro functions exist (Refer Section 4.2) in the hydroxydinitroketone (74).[64] For compound (109) there is evidence of intramolecular hydrogen bonding. In the structure (109), the O(1)-O(6) distance is 2.61Å, the HO(6)-O(1) distance is 1.96Å and the O(1)-C(1)-C(6)-O(6)-HO(6) system is nearly planar as indicated by the torsional angles: O(1)-C(1)-C(6)-O(6) $9.6(5)^{o}$ and C(1)-C(6)-O(6)-HO(6) $O(3)^{o}$. Computer generated packing plots of the crystal unit cell indicate the absence of an extended hydrogen bonding network in the crystal. In compound (109) the aromatic ring is orientated at approximately right-angles to the C(2)-O(2) bond as indicated by the relevant torsional angles: C(2)-O(2)-C(13)-C(18) $-90.6(4)^{o}$ and C(2)-O(2)-C(13)-C(14) $95.7(4)^{o}$.

Notwithstanding the low accountability of products from the reaction in which the hydroxynitrophenoxyketone (109) was produced, some of the experimental conditions under which it is formed were determined.[71] Immediately after the addition of the nitrogen dioxide solution, a ^{1}H n.m.r. spectrum of the reaction mixture was consistent with the presence of equimolar amounts of the phenol (66) and the 4-nitrodienone (77), but compound (109) was formed slowly and after 24h, the ^{1}H n.m.r. spectrum of the mixture was essentially identical with that of

the oily residue obtained, above, by removal of the benzene solvent under reduced pressure.

A solution of the pure 4-nitrodienone (77)[64] in benzene did not yield compound (109), nor did a solution of the pure 4-nitrodienone (77) in benzene to which an equimolar amount of the phenol (66) had been added. Finally, 4-t-butyl-2,6-dimethylphenol (66) was reacted with nitrogen dioxide (2 mole-equivalents) in benzene to form the 4-nitrodienone (77). An aliquot of this benzene solution was extracted with water, and the presence of nitrous acid demonstrated by the Griess-Ilosvay test.[72] To the remaining benzene solution was added the phenol (66) (1 mole-equivalent) and the resulting solution examined by ^{1}H n.m.r. spectroscopy. Under these conditions the hydroxynitrophenoxyketone (109) was formed in a yield *c.* 25%.

CHAPTER 6

EXPERIMENTAL METHODS

6.1 APPARATUS, MATERIALS AND INSTRUMENTATION

Infrared spectra were recorded on a Shimadzu IR-27G spectrophotometer for liquid films and nujol mulls. Ultraviolet absorption spectra were determined for cyclohexane, chloroform, ethanol or methanol solutions on Varian Superscan 3 or Varian DMS 100 spectrophotometers.

Routine ^{1}H n.m.r. spectra were obtained for carbon tetrachloride, deuteriochloroform, deuterioacetonitrile and deuterioacetone solutions, with tetramethylsilane as an internal reference on a Varian T60 spectrometer. ^{1}H n.m.r. and ^{13}C n.m.r. Fourier Transform spectra were recorded on a Varian CFT-20 Fourier Transform NMR spectrometer for deuteriochloroform and deuterioacetone solutions with tetramethylsilane as an internal reference. N.M.R. spectral parameters were derived by first-order analysis and, wherever required and possible, confirmed by double irradiation experiments. All chemical shifts are expressed as parts per million (ppm) downfield from TMS and are quoted as position (δ), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), relative integral and coupling constants (J, Hz).

Microanalyses were carried out by Professor A.D. Campbell and associates, University of Otago.

Melting points were determined in open capillaries and are uncorrected.

Preparative scale chromatography was routinely carried out utilising a Chromatotron (a preparative, centrifugally

accelerated, radial, thin-layer chromatograph. Model 7924, Harrison Research Inc.) equipped with rotors coated with Silica gel PF-254 (with $CaSO_4.\frac{1}{2}H_2O$ type 60 for TLC, Merck: E.M. Laboratories Incorporated, item number 7749) of various thicknesses (generally 2mm).

All solvents used were either of analytical grade (AR) or were purified and dried according to standard procedures.[73] "Ether" refers to commercial diethyl ether distilled off sodium hydride, and "Petroleum ether" refers to petroleum ether (50-70°C) distilled off phosphorus pentoxide.

6.2 EXPERIMENTAL SECTION RELATING TO CHAPTER 2

1,3,5-Trichloro-2,4,6-trimethylbenzene (32)[43]

Through a mixture of 1,3,5-trimethylbenzene (30g), Iron dust (H_2-reduced; 1g) and Ferric chloride (anhydrous; 1g) in carbon tetrachloride (150 ml), heated to 77°, was passed dry chlorine gas at such a rate that complete ring chlorination was achieved after *c*. 3h (as determined by ^{1}H n.m.r.). Excess chlorine was removed by a stream of nitrogen and the reaction mixture was washed with water to remove iron salts. The organic layer was dried and filtered and the solvent removed under reduced pressure to give a crude material which was crystallised from ethanol to give 1,3,5-trichloro-2,4,6-trimethylbenzene (32) (41g; 74%) as fine white needles, m.p. 205-206° (lit.[44] 204°); ^{1}H n.m.r. (CCl_4) δ2.50, methyl protons.

Nitration of 1,3,5-trichloro-2,4,6-trimethylbenzene (32)

To a stirred solution of 1,3,5-trichloro-2,4,6-trimethylbenzene (32)(5g) in dichloromethane (30 ml) at 0-5° was added dropwise fuming nitric acid (11 ml;d 1.5) over 30 min, and the resulting solution stirred for 65h at 20°. The solvents were removed under reduced pressure at 20° to give a yellow solid residue, (*c*. 7.5 g); ν_{max} (nujol) 3500, 1760-1750, 1585-1560 cm^{-1}; ^{1}H n.m.r. ($CDCl_3$) δ1.65, 1.68, 2.15, 2.22, 2.25, 2.28, methyl protons; ^{1}H n.m.r. integrals were consistent with the presence of two compounds, shown to be (42) and (43),[43] in a ratio of *c*. 1:1 .

Fractional crystallisation of the crude product from dichloromethane/pentane mixtures gave first 3,*t*-5-dichloro-*c*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (42),[43]

m.p. 133.5-134.5°(lit.[41] 131-135°)(Found: C, 34.3; H, 3.2; Cl, 22.8; N, 8.9. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 8.9%); ν_{max}(nujol) 3520, OH; 1750, α-nitroketone; 1626, C=C; 1582, 1570 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.65, 2.15, 2.28, each 3H, methyl protons; 4.00, OH (lit.[41] δ 1.61, 2.12, 2.24, methyls; 2.30, OH); ^{13}C n.m.r. (CD_3COCD_3, -25°) satisfactory spectra could not be obtained.

The second compound obtained by fractional crystallisation from dichloromethane/pentane was 3,*c*-5-dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (43),[43] m.p. 104.5-105° (Found: C, 34.2; H, 3.4; Cl, 22.8; N, 8.7. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 8.9%); ν_{max}(nujol) 3500, OH; 1760, α-nitroketone; 1635, C=C; 1578, 1565 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.68, 2.22, 2.25, each 3H, methyl protons; 3.80, OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) satisfactory spectra could not be obtained.

Base-Catalysed Acyloin Rearrangements of 6-hydroxy-6-methyl-2,5-dinitrocyclohex-3-enones (8),(10),(29),(30),(42) and (43).[43]

General Procedure[43] - A two-phase system consisting of a solution of the 6-hydroxy-6-methyl-2,5-dinitrocyclohex-3-enone in dichloromethane (2% w/v) and aqueous sodium bicarbonate (0.7% w/v; 25 ml/g ketone) was vigorously agitated for an appropriate period. The organic layer was separated, dried with magnesium sulphate, and evaporated at 20° to give a residue, the components of which were separated by fractional crystallisation from dichloromethane/pentane and ether/pentane mixtures.

r-2,4,*c*-5-Tribromo-*t*-6-hydroxy-3,6-dimethyl-2,5-dinitrocyclohex-3-enone (8)

(A) 30s: Treatment of the ketone (8) (100 mg),[37,38] as above,

for 30s gave a crude product (95 mg), shown by ^{1}H n.m.r. to be a mixture (*c.* 4.5:1) of the two acyloin rearrangement products (9) and (45). Crystallisation from dichloromethane/pentane gave 1-acetyl-*c*-2,4,*c*-5-tribromo-3-methyl-2,5-dinitrocyclopent-3-en-*r*-1-ol (9), m.p. 141-142° (dec.)[lit.[37] 141°(dec)], ν_{max}(nujol) 3480, OH; 1716, C=O; 1620, C=C; 1580, 1570 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 2.35, 2.36, each 3H, methyl protons; *c.* 4.6, D_2Oexch., OH; identical with an authentic sample.[37,38]

(B) 20min: Treatment of the ketone (8) (2.4g), as above, for 20 min gave a crude product (2.23g) shown, by ^{1}H n.m.r., to be a mixture (*c.* 2.9:1) of the two acyloin rearrangement products (9) and (45). Fractional crystallisation from dichloromethane/pentane gave first compound (9), identical with the above. Repeated crystallisations of the residue from dichloromethane/pentane and finally from ether/pentane gave the isomeric 1-acetyl-*t*-2,4,*t*-5-tribromo-3-methyl-2,5-dinitrocyclopent-3-en-*r*-1-ol (45), m.p. 117-118°(dec.), (Found: C, 20.7; H, 1.6; Br, 51.1; N, 5.7. $C_8H_7Br_3N_2O_6$ requires C, 20.6; H, 1.5; Br, 51.4; N, 6.0%); ν_{max}(nujol) 3475, OH; 1746, 1740, C=O; 1620, C=C, 1570 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 2.30, 2.64, each 3H, methyl protons; *c.* 5.7, D_2O exch., OH; ^{13}C n.m.r. (CD_3COCD_3; -25°) satisfactory spectra could not be obtained.

3,4,*t*-5-Tribromo-*c*-6-hydroxy-2,6-dimethyl-*r*-2,5-dinitrocyclohex-3-enone (29)

Treatment of the ketone (29)(1.5g),[40] as above, for 30s gave a crude product (1.35g), shown by ^{1}H n.m.r. to be a mixture (*c.* 1:1:1) of the ketone (29) and the acyloin rearrangement products (46) and (47). Fractional crystallisation

of this material from dichloromethane/pentane gave first 1-acetyl-3,4,*c*-5-tribromo-2-methyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (46), m.p. 139-140°(dec.) (Found: C, 20.8; H, 1.6; Br, 52.0; N, 5.9. $C_8H_7Br_3N_2O_6$ requires C, 20.6; H, 1.5; Br, 51.4; N, 6.0%). ν_{max}(nujol) 3500, OH; 1719, C=O; 1593, C=C; 1563, 1553 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.95, 2.30; each 3H, methyl protons; *c*. 4.75, D_2Oexch., OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 20.2, 2-CH_3; 27.3, CO-$\underline{C}H_3$; 89.5, C1; 89.9, C2; 100.4, C5; 129.4, C4; 134.1, C3; 203.1, C=O.

Further fractional crystallisation first from dichloromethane/pentane and then ether/pentane gave 1-acetyl-3,4,*t*-5-tribromo-2-methyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (47), m.p. 120-121°(dec.) (Found: C, 20.8; H, 1.9; Br, 51.3; N, 5.7. $C_8H_7Br_3N_2O_6$ requires C, 20.6; H, 1.5; Br, 51.4; N, 6.0%); ν_{max} (nujol) 3400(br), OH; 1720(br), C=O; 1585, 1560 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.78, 2.53, each 3H, methyl protons; *c*. 5.5, D_2O exch., OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 21.2, 2-CH_3; 29.2, CO-$\underline{C}H_3$; 87.7, C1; 99.4, C2; 100.1, C5; 131.5, C4; 135.4, C3; 203.4, C=O.

r-2,3,4,*c*-5-Tetrabromo-*t*-6-hydroxy-6-methyl-2,5-dinitrocyclohex-3-enone (10)

Treatment of the ketone (10) (645mg),[38] as above, for 5 min gave a crude product (586mg), shown by ^1H n.m.r. to be a mixture (*c*. 1:1) of the two acyloin rearrangement products (11) and (48). Similar reactions for 10s and 30s also gave a mixture (*c*. 1:1) of these products. Fractional crystallisation of this material from dichloromethane/pentane gave first 1-acetyl-*c*-2,3,4,*c*-5-tetrabromo-2,5-dinitrocyclopent-3-en-*r*-1-ol (11), m.p. 141°(dec.)(lit.[38]140-141°); ν_{max} (nujol) 3475, OH; 1725, C=O; 1585, 1560 cm^{-1}, NO_2; ^1H n.m.r. (CD_3COCD_3) δ 2.43,

methyl; ($CDCl_3$) δ 2.38, methyl; *c*. 4.7, OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 23.9, methyl; 86.5, C1; 98.5, C2 and C5; 128.2, C3 and C4; 199.8, C=O; identical with an authentic sample.[38]

Repeated crystallisation of the residue from above from dichloromethane/pentane gave 1-acetyl-*t*-2,3,4,*t*-5-tetrabromo-2,5-dinitrocyclopent-3-en-*r*-1-ol (48), m.p. 109-110°(dec.) (Found: C, 15.8; H, 1.0; Br, 59.7; N, 5.1. $C_7H_4Br_4N_2O_6$ requires C, 15.8; H, 0.8; Br, 60.1; N, 5.3%); ν_{max}(nujol) 3455(br), OH; 1746, 1733, C=O; 1583 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 2.63, methyl; *c*. 5.8, OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 31.0, methyl; 89.8, C1; 99.6, C2 and C5; 135.1, C3 and C4; 200.0, C=O.

3,*t*-5-Dichloro-*c*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (42)

(A) 5 min: Treatment of the ketone (42)(1g),[43] as above, for 5 min gave a crude product (975mg), shown by ^1H n.m.r. to be a mixture (*c*. 5:4) of the ketone (42) and the acyloin rearrangement product (49). Fractional crystallisation of this material from dichloromethane/pentane gave the ketone (42), identical with an authentic sample, and 1-acetyl-3,*c*-5-dichloro-2,4-dimethyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (49) m.p. 152.5-153°(dec.) (Found: C, 34.5; H, 3.3; Cl, 22.6; N, 8.8. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 9.0%.) [lit.[41] 153-154°(dec.) for the compound assigned structure (34)]; ν_{max}(nujol) 3440(br), OH; 1715, C=O; 1650, C=C; 1572, 1560 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.89, 2.24, 2.27, each 3H, methyl protons; *c*. 4.5, D_2O exch., OH (lit.[41] values δ 1.79, 2.24, 2.27, *c*.4.5); ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 12.9, 4-CH_3; 19.6, 2-CH_3; 27.4, CO-$\underline{C}H_3$; 89.9, C1; 100.0, C2; 111.4, C5; 137.1, C3/C4; 138.7, C4/C_3; 203.6, C=O.

(B) 30 min: Treatment of the ketone (42)(1g), as above, for 30 min gave a crude product (931mg), shown by ^{1}H n.m.r. to be a mixture (*c.* 1:1:1.5) of the ketone (42) and the two acyloin rearrangement products (49) and (50). Fractional crystallisation of this material from dichloromethane/pentane gave the ketone (42) and the acyloin rearrangement product (49), identical with authentic material. Continued fractional crystallisation first from dichloromethane/pentane and then ether/pentane gave 1-acetyl-3,*t*-5-dichloro-2,4-dimethyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (50), m.p. 113-114°(dec.) (Found: C, 34.7; H, 3.3; Cl, 23.0; N, 8.8. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 9.0%); ν_{max}(nujol) 3400(br), OH; 1725, C=O; 1640, C=C; 1577, 1563 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.75, 2.13, 2.50, each 3H, methyl protons; *c.* 5.4, D_2O exch., OH; ^{13}C n.m.r., satisfactory spectra could not be obtained.

3,*c*-5-Dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2, 5-dinitrocyclohex-3-enone (43)

(A) 1 min: Treatment of the ketone (43)(1g),[43] as above, for 1 min gave a crude product (992mg), shown by ^{1}H n.m.r. to be a mixture (*c.* 5:5:3) of the ketone (43) and the acyloin rearrangement products (51) and (44). Fractional crystallisation of this material from dichloromethane/pentane gave 1-acetyl-3,*c*-5-dichloro-2,4-dimethyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (51), m.p. 137-138°(dec.) (Found: C, 34.5; H, 3.6; Cl, 22.9; N, 8.9. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 9.0%); ν_{max} (nujol) 3450(br), OH; 1723, C=O; 1655, C=C; 1573, 1565 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.73, 2.33, 2.45, each 3H, methyl protons; *c.* 4.3, D_2O exch. , OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 13.4, 4-CH_3; 18.4, 2-CH_3; 29.0, CO-$\underline{C}H_3$; 88.2, C1; 100.1, C2; 111.1, C5; 136.3, C3; 141.6, C4; 208.8, C=O.

(B) 30 min: Treatment of the ketone (43)(1g), as above, for 30 min gave a crude product (990mg), shown by ^{1}H n.m.r. to be a mixture (*c.* 1:1:2) of the ketone (43) and the acyloin rearrangement products (51) and (44). Fractional crystallisation first from dichloromethane/pentane and then ether/pentane gave 1-acetyl-3,*t*-5-dichloro-2,4-dimethyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (44), m.p. 116.5-118°(dec.) (Found: C, 34.7; H, 3.2; Cl, 22.9; N, 9.0. $C_9H_{10}Cl_2N_2O_6$ requires C, 34.5; H, 3.2; Cl, 22.7; N, 9.0%); ν_{max}(nujol) 3430, OH; 1737, C=O; 1653, C=C; 1587, 1565 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.94, 2.01, 2.24, each 3H, methylprotons; *c.* 5.4, D_2O exch., OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 11.4, 4-CH_3; 21.8, 2-CH_3; 29.0, CO-$\underline{C}H_3$; 89.6, C1; 90.4, C2; 100.4, C5; 137.6, C3/C4; 138.6, C4/C3; 205.2, C=O; the structure of compound (44) was determined by X-ray crystal structure analysis.[43] (See Appendix).

3,4,*c*-5-Tribromo-*t*-6-hydroxy-2,6-dimethyl-*r*-2,5-dinitrocyclohex-3-enone (30)

Treatment of the ketone (30)(1g),[40] as above, for 30s gave a crude product (974mg), shown by ^{1}H n.m.r. to be a mixture (*c.* 1:1.7) of the acyloin rearrangement products (52) and (53). Fractional crystallisation from dichloromethane/pentane and finally from ether/pentane gave 1-acetyl-3,4,*c*-5-tribromo-2-methyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (52), m.p. 138-139°(dec.) (Found: C, 20.5; H, 1.6; Br, 51.2; N, 5.8. $C_8H_7Br_3N_2O_6$ requires C, 20.6; H, 1.5; Br, 51.4; N, 6.0%); ν_{max} (nujol) 3450, OH; 1728, 1720, C=O; 1592, C=C; 1570, 1560 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.74, 2.43, each 3H, methyl protons; *c.* 4.5, D_2O exch., OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 20.1, 2-CH_3; 30.2, CO-$\underline{C}H_3$; 87.5, C1; 87.9, C2; 101.0, C5; 125.7, C4; 133.6, C3; 208.2, C=O.

Further fractional crystallisation from ether/pentane gave

1-acetyl-3,4,*t*-5-tribromo-2-methyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (53), m.p. 129-130°(dec.) (Found: C, 21.1; H, 1.9; Br, 51.0; N, 5.6; $C_8H_7Br_3N_2O_6$ requires C, 20.6; H, 1.5; Br, 51.4; N, 6.0 %); ν_{max} (nujol) 3460(br), OH; 1723, C=O; 1593, C=C; 1580, 1558 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.97, 2.30, each 3H, methyl protons; *c*. 5.5, D_2O exch. , OH; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 22.6, 2-CH_3; 27.6, CO-$\underline{C}H_3$, 87.6, C1; 89.5, C2; 101.4, C5; 125.6, C4; 135.8, C3; 205.3, C=O.

Base-Catalysed Acyloin Rearrangement of 1-Acetyl-3,*c*-5-dichloro-2,4-dimethyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (49)

Treatment of the cyclopentenol derivative (49)(70mg)[43] for 5 min, as above, gave a crude product (69mg) shown, ^1H n.m.r., to be a mixture (*c*. 1:1:1.5) of the cyclohex-3-enone derivative (42) and the two cyclopentenol derivatives (49) and (50).

Base-Catalysed Acyloin Rearrangement of 1-Acetyl-3,*c*-5-dichloro-2,4-dimethyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (51)

Treatment of the cyclopentenol derivative (51)(20mg)[43] for 1 min, as above, gave a crude product (20mg) shown, ^1H n.m.r. to be a mixture (*c*. 5:5:4) of the cyclohex-3-enone derivative (43) and the two cyclopentenol derivatives (51) and (44).

Rearrangement of 1-acetyl-3,*t*-5-dichloro-2,4-dimethyl-*c*-2,5-dinitrocyclopent-3-en-*r*-1-ol (50) in (D_6)-Acetone

The cyclopentenol (50)(50mg),[43] m.p. 113-114°(dec.). ν_{max} (nujol) 3400(br), OH; 1725, C=O; 1640, C=C, 1577, 1563 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.75, 2.13, 2.50, each 3H, methyl protons, *c*. 5.4, D_2O exch., OH, was dissolved in (D_6)-acetone at -78° and ^{13}C and ^1H n.m.r. spectra obtained at -25°. These spectra indicated the presence of two compounds in a ratio *c*. 2:3

(^{1}H n.m.r. integrals). Minor component (54): ^{1}H n.m.r. (CD_3COCD_3) δ 1.53, 1.83, 3.05, all 3H, methyl protons; 7.13, OH; ^{13}C n.m.r. (CD_3COCD_3) δ 17.4, 18.2, 24.7, 79.3, 87.1, 97.3, 132.6, 138.5, 196.9. Major component (50): ^{1}H n.m.r. (CD_3COCD_3) δ 2.14, 2.23, 2.53, all 3H, methyl protons; 7.10, OH; ^{13}C n.m.r. (CD_3COCD_3) δ 12.1, 20.1, 29.5, 79.3, 87.9, 99.3, 125.7, 140.5, 203.3. Removal of the solvent under reduced pressure from the above solution, which had been kept at 20° for 2h, gave a crude product (46mg). ν_{max}(nujol) 3500(sh), OH; 3400(br), OH; 1760, α-nitro ketone; 1725, C=O; 1640, C=C; 1575, 1563 cm^{-1}, NO_2.

Fractional crystallisation of this material from dichloromethane/pentane gave first 3,*t*-5-dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (54) (18mg),[45] m.p. 130-132°(dec.), m.m.p. with (42) 116-120°(dec.); ν_{max} (nujol) 3500(sh), OH; 1760, α-nitroketone; 1642, C=C; 1572, 1563 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.62, 2.13, 2.18, all 3H, methyl protons; *c*. 3.3, OH; the structure of compound (54) was determined by X-ray crystal structure analysis[45] (See Appendix).

Continued fractional crystallisation of the residue from above from dichloromethane/pentane gave the cyclopentenol derivative (50), m.p. and m.m.p. with authentic material[43] 113-114°(dec.); ν_{max}(nujol) 3400(br), OH; 1725, C=O; 1640, C=C; 1577, 1563 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.75, 2.13, 2.50, all 3H, methyl protons; *c*. 5.4, OH.

Treatment of 3,*t*-5-dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (54) with aqueous Sodium bicarbonate/Dichloromethane

The dinitrocyclohex-3-enone (54)(3mg) in dichloromethane (2ml) was shaken with aqueous sodium bicarbonate (2ml; 0.7% w/v) for 15 min. The dichloromethane layer was separated, dried and

the solvent removed under reduced pressure to give an oil (3mg), shown (^{1}H n.m.r.) to be a mixture (*c.* 1:1:1) of the dinitrocyclohex-3-enone (42) and the two cyclopentenol derivatives (49) and (50);[43] the dinitrocyclohex-3-enone (54) could not be detected in the mixture.

6.3 EXPERIMENTAL SECTION RELATING TO CHAPTER 3

Reaction of 2,3,4,5-tetrabromo-6-methylphenol (2) with nitrogen dioxide in cyclohexane[60]

A suspension of the phenol (2)(255mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred suspension for 30s, and stirring continued for a further 2h while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate was isolated by filtration and identified (i.r., ^{1}H n.m.r., mixed m.p.) as the *cis*-dinitroketone (10)(208mg), m.p. 93-94.5°(dec.).[38] Removal of the solvent from the filtrate under reduced pressure gave a residue (70mg) shown (i.r., ^{1}H n.m.r.) to be slightly impure *cis*-dinitroketone (10).

Reaction of 2,4,5-tribromo-3,6-dimethylphenol (5) with nitrogen dioxide in cyclohexane[60]

A suspension of the phenol (5)(500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the suspension for 30s, and stirring continued for a further 2h while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. A precipitate appeared after 5 min. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate was isolated by filtration and identified (i.r., ^{1}H n.m.r., mixed m.p.) as the *cis*-dinitroketone (8)(462mg).[38] Removal of solvent from the filtrate under reduced pressure gave a residue (109mg) shown by ^{1}H n.m.r. to contain *c*. 25% of 2,5-dibromo-3,6-dimethylbenzo-1,4-quinone and *c*. 25% of the

cis-dinitroketone (8).

Reaction of 3,4,5-tribromo-2,6-dimethylphenol (28) with nitrogen dioxide in cyclohexane[60]

Reaction time 2h. - A suspension of the phenol (28)(500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred suspension for 1 min, and stirring continued for a further 2h while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. The solution was initially green in colour and the phenol dissolved ater 1.5-2 min; a precipitate began forming after 3 min. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate was isolated by filtration and identified (i.r., ^{1}H n.m.r.) as a mixture (504mg), 2.1:1, total 77%) of the *cis*-(29) and *trans*-(30) 6-hydroxy-2,5-dinitrocyclohex-3-enones.[40] Removal of the solvent from the filtrate under reduced pressure gave a residue (64mg), shown by i.r. and ^{1}H n.m.r. to be a mixture (*c.* 2:3) of the *cis*-(29) and *trans*-(30) dinitroketones above.

Reaction time 15.5h. - Reaction of the phenol (28)(500mg), as above, except that stirring of the reaction mixture was continued for 15.5h, gave a precipitate (470mg) which was identified (^{1}H n.m.r.) as a mixture (*c.* 2:1) of the *cis*-(29) and *trans*-(30) dinitroketones. The residue (104mg) was shown by i.r. and ^{1}H n.m.r. to be a mixture (*c.* 1:7) of the *cis*-(29) and *trans*-(30) dinitroketones.

Reaction time 1.5 min. - Reaction of the phenol (28)(100mg) in cyclohexane (5ml), as above, except that stirring of the reaction mixture was continued for a total reaction time of 1.5 min. A small amount of solid remained (11mg) at the end of the reaction and was identified (i.r. and ^{1}H n.m.r.) as

unchanged phenol (28). Removal of the solvent from the filtrate under reduced pressure gave a yellow oil (118mg) shown by ^{1}H n.m.r. to consist of a mixture of the *cis*-(29) and *trans*-(30) dinitroketones, the 4-nitrodienone (55),[61] the 6-nitrodienone (56) and the 6-hydroxydienone (31)[40] in a ratio *c*. 3:2:6:6:7 respectively.

Reaction of 3,4,5-tribromo-6-hydroxy-2,6-dimethylcyclohexa-2,4-dienone (31) with nitrogen dioxide in cyclohexane[60]

A suspension of the 6-hydroxydienone (31)[40] (450mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred suspension for 30s, and stirring continued for a further 2h while the mixture was stored at 10^{o} under an atmosphere of nitrogen dioxide. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate was isolated by filtration and identified (i.r. and ^{1}H n.m.r.) as being essentially pure *cis*-dinitroketone (29)[40] (272mg). The residue (235mg) from the removal of solvent from the filtrate under reduced pressure was shown (i.r. and ^{1}H n.m.r.) to be a mixture (*c*. 1:8) of the *cis*-(29) and *trans*-(30) dinitroketones.[40]

Reaction of 3,5-dichloro-2,4,6-trimethylphenol (41) with nitrogen dioxide in cyclohexane[60]

A suspension of the phenol (41) (500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred suspension for 30s, and stirring continued for a further 88h while the mixture was stored at *c*. 20^{o} under an atmosphere of nitrogen dioxide. After 88h the excess nitrogen dioxide was removed in a stream of dry nitrogen and the precipitate (411mg) was isolated by

filtration and identified by i.r. and ^{1}H n.m.r. as a mixture (*c.* 3:2) of the *cis*-(42) and *trans*-(43) dinitroketones.[43] The residue (360mg) was an oil, and was shown by ^{1}H n.m.r. to be a complex mixture, in which the *trans*-dinitroketone (43) was a minor component.

Reaction of 2,4-dibromo-3,5,6-trimethylphenol (57) with nitrogen dioxide in cyclohexane[60]

A suspension of the phenol (57) (500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the vigorously stirred, cooled ($<10^{\circ}$) suspension for 30s, and stirring continued for a further 2h while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. The solution was initially green in colour and a precipitate began forming after 3 min. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate was isolated by filtration. The solid was shown (i.r.) to be a mixture (598mg, *c.* 1:1, total 87%) of the isomeric trinitroketones (58a) and (58b),[60] m.p. 90-107°(dec). ν_{max}(nujol) 1762, α,α'-dinitro ketones; 1622, C=C; 1615, C=C; 1587, 1560-1570 cm^{-1}, NO_2. ^{1}H n.m.r. ($CDCl_3$) δ 2.10, 2.22, 2.23, all 3H, methyl protons, trinitroketone (58a); signals at 1.51, 1.71, 1.83, 1.95, 2.03, 2.05, 2.17, 2.27, 2.58, trinitroketone(s) (58b) and/or rearrangement products; ^{13}C n.m.r. (CD_3COCD_3, -25°) satisfactory spectra could not be obtained. (Found: C, 25.2; H, 2.4; Br, 36.7; N, 9.6. $C_9H_9Br_2N_3O_7$ requires C, 25.1; H, 2.1; Br, 37.1; N, 9.7%).

Removal of solvent under reduced pressure from the cyclohexane solution above, gave an oily residue (90mg) which appeared (i.r., ^{1}H n.m.r.) to be a complex mixture.

Reaction of 2,4-dibromo-3,5,6-trimethylphenol (57) with nitrogen dioxide in Acetic acid[60]

A suspension of the phenol (57)(500mg) in glacial acetic acid (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the vigorously stirred suspension (at *c.* 10°) for 30s, and stirring continued for a further 2h while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. The solution was initially green in colour and a precipitate began forming after 8 min. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the precipitate isolated by filtration. The solid was shown to be the trinitroketone (58a)(300mg; 44%),[60] m.p. 102-103°(dec.) ν_{max}(nujol) 1760, α,α'-dinitroketone; 1615, C=C, 1587, 1560-1570 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 2.10, 2.22, 2.23, all 3H, methyl protons.

Removal of the solvent, under reduced pressure, from the filtrate gave a solid residue (337mg) shown by ^1H n.m.r. and infrared spectra to be a mixture (*c.* 1:1) of the C2-epimeric hydroxydinitroketones (59) and (60);[60] the yields of these compounds were each estimated to be *c.* 24%.

6.4 EXPERIMENTAL SECTION RELATING TO CHAPTER 4

4-t-Butyl-2,6-dimethylphenol (66)

A solution of 2,6-dimethylphenol (74g), t-butyl alcohol (55g; 1.25 molar-equivalents) and concentrated phosphoric acid (85% w/v; 242g) was placed in a 1-litre three-neck round-bottom flask fitted with a reflux condenser and a mechanical stirrer.[74] With the stirrer operating at a speed sufficient to mix the two layers thoroughly, the solution was heated at 80-90^{o} for 48h.

The solution was then cooled to room temperature and extracted with light petroleum (3x100ml). The light petroleum extracts were washed free of acid with water (as tested by blue litmus paper), dried, and evaporated under reduced pressure to give a viscous pale-orange liquid (105g; 97%) shown (^{1}H n.m.r.) to be essentially pure 4-*t*-butyl-2,6-dimethylphenol (66).

Crystallisation of the above crude material from a minimum amount of light petroleum yielded two crops of pure 4-t-butyl-2,6-dimethylphenol (66)(total 50.6g; 47%) m.p. 81-82^{o} (lit.[63a] 82.4^{o}); ν_{max}(nujol) 3350(br), OH; 1605 cm^{-1}, aromatic; ^{1}H n.m.r. ($CDCl_3$) δ 1.28, s, 9H, t-butyl; 2.23, s, 6H, methyls; *c.* 4.5, s, 1H, D_2O exch., OH, 6.98, s, 2H, H3, H5; ^{13}C n.m.r. ($CDCl_3$) δ 16.11, methyls; 31.61, t-butyl methyls; 33.87, $\underline{C}$-Me_3; 122.43, C2, C6; 125.48, C3, C5; 142.87, C4; 149.89, C1.

Reaction of 4-t-butyl-2,6-dimethylphenol (66) with nitrogen dioxide in benzene[64]

A solution of the phenol (66)(500mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10^{o} for 30s and stirring continued for 2h while the mixture was stored

at 20° under an atmosphere of nitrogen dioxide. The solution remained green in colour during the 2h period. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a pasty solid (910mg) shown (^{1}H n.m.r.), to be a mixture of (70),(71), (72),(73) and (74)(*c.* 4:2:2:1:1).

Separation of the crude mixture was achieved using a Chromatotron equipped with a silica-gel PF-254 plate. Separated components were further purified by recrystallisation from either dichloromethane/pentane or ether/pentane mixtures.

Elution with petroleum ether/ether (50:50) gave 4-t-butyl-2,6-dimethyl-*r*-2,*t*-5,*c*-6-trinitrocyclohex-3-enone (70) as a colourless crystalline solid, m.p. 113-113,5°(dec.); (Found: C, 45.6, H, 5.6; N, 13.1. $C_{12}H_{17}N_3O_7$ requires C, 45.7; H, 5.4; N, 13.3%); ν_{max}(nujol) 1755, α,α'-dinitroketone; 1653, C=C; 1570-1555(br) cm^{-1}, NO_2; ^{1}H n.m.r. (CD_3CN) δ 1.23, s, 9H, t-butyl; 1.86, s, 3H, methyl; 2.06, s, 3H, methyl; 6.40, d, 1H, $J_{5,3}$ 1.5Hz, H5; 6.67, d, 1H, $J_{3,5}$ 1.5Hz, H3; ^{13}C n.m.r. (CD_3COCD_3): not obtainable at -25°.

Elution with petroleum ether/ether (25:75) gave 4-t-butyl-2,6-dimethyl-*r*-2,*c*-5,*t*-6-trinitrocyclohex-3-enone (71) as a colourless crystalline solid, m.p. 101-101.5°(dec); ν_{max} (nujol) 3100, olefinic C-H; 1757, α,α'-dinitroketone; 1650, C=C; 1575, 1560, 1555 cm^{-1}, NO_2; ^{1}H n.m.r. (CD_3CN) δ 1.23, s, 9H, t-butyl; 1.90, s, 3H, methyl; 2.01, s, 3H, methyl; 6.33, d, 1H, $J_{5,3}$ 1.5Hz, H5; 6.52, d, 1H, $J_{3,5}$ 1.5Hz, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 19.37, C-6 methyl; 28.41, t-butyl methyls; 28.70, C-2 methyl; 37.80, $\underline{C}$-Me_3; 88.02, C2/C5/C6; 89.30, C5/C6/C2; 91.63, C6/C2/C5; 129.48, C3; 144.30, C4; 187.21, C1; the structure of the trinitroketone (71) was determined by X-ray crystal structure analysis (See Appendix).

Elution with ether gave 4-t-butyl-2,6-dimethyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (72) as a colourless crystalline solid, m.p. 135.5-136°(dec.); ν_{max}(nujol) 3100, olefinic C-H; 1760, α,α'-dinitroketone; 1650, C=C; 1580, 1570, 1555 cm^{-1}, NO_2; ^1H n.m.r. (CD_3CN) δ 1.25, s, 9H, t-butyl; 1.96, s, 3H, methyl; 2.07, s, 3H, methyl; 6.22, d, 1H, $J_{5,3}$ 1.5Hz, H5; 6.53, d, 1H, $J_{3,5}$ 1.5Hz, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 21.25, C-2 methyl/C-6 methyl; 23.07, C-6 methyl/C-2 methyl; 28.37, t-butyl methyls; 38.26, $\underline{C}$-Me_3; 88.48, C2/C5/C6; 91.91, C5/C6/C2; 95.88, C6/C2/C5; 128.71, C3; 145.38, C4; 189.38, C1; the structure of trinitroketone (72) was determined by X-ray crystal structure analysis (See Appendix).

Elution with methanol gave 4-t-butyl-*c*-6-hydroxy-2,6-dimethyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (74) as a colourless crystalline solid, m.p. 131-132°(dec.); ν_{max}(nujol) 3500, OH; 1745, α-nitroketone; 1655, C=C; 1575, 1557 cm^{-1}, NO_2; ^1H n.m.r. (CD_3CN) δ 1.23, s, 9H, t-butyl; 1.46, s, 3H, C-6 methyl; 1.95, s, 3H, C2 methyl; 5.72, d, 1H, $J_{5,3}$ 1.7Hz, H5; 6.42, d, 1H, $J_{3,5}$ 1.7Hz, H3; ^{13}C n.m.r. (CD_3COCD_3): not obtainable at -25°; the structure of hydroxydinitroketone (74) was determined by X-ray crystal structure analysis (See Appendix).

Further elution with methanol gave 4-t-butyl-2,6-dimethyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (73) as a colourless crystalline solid, m.p. 136.5-137°(dec.); ν_{max}(nujol) 1760, α,α'-dinitroketone; 1655, C=C; 1570(br), 1550 cm^{-1}, NO_2; ^1H n.m.r. (CD_3CN) δ 1.27, s, 9H, t-butyl; 1.93, s, 3H, methyl; 2.01, s, 3H, methyl; 6.15, d, 1H, $J_{5,3}$ 1.7Hz, H5; 6.40, d, 1H, $J_{3,5}$ 1.7Hz, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 21.42, C-6 methyl; 27.53, C-2 methyl; 28.39, t-butyl methyls; 38.09, $\underline{C}$-Me_3; 87.41, C2/C5/C6; 90.33, C5/C6/C2; 95.89, C6/C2/C5; 128.12, C3; 145.03,

C4; 188.91, Cl; the structure of trinitroketone (73) was determined by X-ray crystal structure analysis (See Appendix).

4-t-Butyl-2,6-dimethyl-4-nitrocyclohexa-2,5-dienone (77)[64]

A. - Fuming nitric acid (0.13ml; d 1.5) was added dropwise to a stirred solution of 4-t-butyl-2,6-dimethylphenol (66) (500mg) in acetic acid (2ml) cooled in an ice-water bath. The solution was then extracted with light petroleum (2x10ml) and the light petroleum extracts washed free of acid with water (3x50ml), dried, and evaporated under reduced pressure to give a pale-yellow oil (598mg) shown (^{1}H n.m.r.), to consist essentially of a single product.

Separation of the crude material on a Chromatotron equipped with a silica-gel PF-254 plate and elution with petroleum ether/ether (80:20) gave 4-t-butyl-2,6-dimethyl-4-nitrocyclohexa-2,5-dienone (77) as an unstable pale-yellow oil, ν_{max} (liquid film) 1675, C=O; 1650 cross-conjugated dienone; 1545 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.12, s, 9H, t-butyl; 1.98, s, 6H, methyls; 7.13, s, 2H, H3, H5; λ_{max} (cyclohexane) 239 nm (ε 9600). All attempts to crystallise the nitrodienone resulted in its decomposition.

B. - A solution of the phenol (66) (500mg) in benzene (3ml) was deoxygenated by a stream of pure nitrogen. A solution of nitrogen dioxide (260mg; 2 molar-equivalents) in benzene (1ml) was added over 30 min to the cooled (*c.* 5°), stirred solution of the phenol under an atmosphere of nitrogen. After the addition was complete, the benzene solvent was removed at 20° under reduced pressure to give a pale-yellow oil (620mg), shown (^{1}H n.m.r.) to consist essentially of a single product.[64]

Separation of the crude material on a Chromatotron, as for A.- gave 4-t-butyl-2,6-dimethyl-4-nitrocyclohexa-2,5-dienone

(77) identical to the material in A).

Reaction of 4-t-butyl-2,6-dimethyl-4-nitrocyclohexa-2,5-dienone (77) with nitrogen dioxide in benzene[64]

A solution of the nitrodienone (77)(297mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution for 30s and stirring continued for 2h while the mixture was stored at 20° under an atmosphere of nitrogen dioxide. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a viscous pale-straw coloured oil (416mg) shown (^{1}H n.m.r., i.r.), to be a mixture of (70),(71),(72),(73) and (74) (*c.* 9:4:4:1:2).

Separation of the crude mixture on a Chromatotron equipped with a silica-gel PF-254 plate and subsequent recrystallisation of the obtained fractions from either dichloromethane/pentane or ether/pentane mixtures gave samples of (70),(71),(72),(73) and (74) identical in all respects (m.p., m.m.p., i.r., ^{1}H n.m.r.) with authentic materials.

2-t-Butyl-4,6-dimethylphenol (79)

A solution of 2,4-dimethylphenol (40g), t-butyl alcohol (30g; 1.25 molar-equivalents) and concentrated phosphoric acid (85% w/v; 130g) was placed in a 500ml three-neck round-bottom flask fitted with a reflux condenser and a mechanical stirrer.[74] With the stirrer operating at a speed sufficient to mix the two layers thoroughly, the solution was heated at 80-90° for 48h.

The solution was then cooled to room temperature and extracted with light petroleum (250ml). The light petroleum extracts were washed free of acid with water (as tested by blue litmus paper), dried, and evaporated under reduced pressure to give a pale-yellow liquid (56.3g) shown (^{1}H n.m.r.) to be essentially pure 2-t-butyl-4,6-dimethylphenol. Fractional distillation of the pale-yellow liquid under diminished pressure yielded pure 2-t-butyl-4,6-dimethylphenol (79) (24.7g; 43%) as a pale-straw coloured liquid, b.p. 120-123° (10mm Hg) (lit.[63b] 115° (10mm Hg)), ν_{max} (liquid film) 3575, OH; 1600 cm^{-1}, aromatic. ^{1}H n.m.r. (CCl_4) δ 1.38, s, 9H, t-butyl; 2.11, s, 3H, C4-methyl; 2.18, s, 3H, C6-methyl; 4.3, s, 1H, D_2O exch., OH; 6.65, bs, 1H, H5; 6.80, bs, 1H, H3.

The phenol (79) oxidised readily in air at room temperature (as evidenced by a deepening yellow colour over time), and so was stored under nitrogen at *c*. 4° while not required.

Reaction of 2-t-butyl-4,6-dimethylphenol with nitrogen dioxide in benzene

A solution of the phenol (79)(1g) in benzene (10ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10° for 30s and stirring continued for 5h while the mixture was stored at 20°

under an atmosphere of nitrogen dioxide. The solution was initially green in colour, the depth of colour decreasing slightly over the 5h reaction period. After 5h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a pale-yellow solid (1790mg) shown (^{1}H n.m.r., i.r.) to be a mixture of the two trinitroketones (80) and (81) (*c.* 1:1).

Fractional crystallisation of the above mixture from dichloromethane/pentane, without heating, gave the pure 2-t-butyl-4,6-dimethyl-*r*-4,*c*-5,*t*-6-trinitrocyclohex-2-enone (80) (410mg), m.p. 141-142°(dec.); ν_{max}(nujol) 1712, conjugated C=O; 1575, 1568, 1555 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.27, s, 9H, t-butyl; 1.93, s, 3H, methyl; 2.07, s, 3H, methyl; 6.08, s, 1H, H5; 6.70, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3) not obtainable at -25°; λ_{max} ($CHCl_3$) 243 nm (ε 6100); the structure of the trinitroketone (80) was determined by X-ray crystal structure analysis (See Appendix).

Removal of the solvent from the mother liquor of the above crystallisation under reduced pressure gave a residue which upon fractional crystallisation from dichloromethane/pentane gave pure 2-t-butyl-4,6-dimethyl-*r*-4,*t*-5,*c*-6-trinitrocyclohex-2-enone (81) (130mg), m.p. 146-147°(dec.); ν_{max}(nujol) 1706, conjugated C=O; 1568(br), 1552 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.27, s, 9H, t-butyl; 1.95, s, 6H, methyls; 6.53, s, 1H, H5; 6.95, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3) not obtainable at -25°; λ_{max} ($CHCl_3$) 243 nm (ε 5400); the structure of the trinitroketone (81) was determined by X-ray crystal structure analysis (See Appendix).

2-t-Butyl-4,6-dimethyl-4-nitrocyclohexa-2,5-dienone (82)[33]

A. - Fuming nitric acid (0.13ml; d 1.5) was added dropwise to a stirred solution of 2-t-butyl-4,6-dimethylphenol (79)(500mg) in acetic acid (2ml) cooled in an ice-water bath. The solution was then extracted with light petroleum (2x10ml) and the light petroleum extracts washed free of acid with water (3x50ml), dried, and evaporated under reduced pressure to give a pale-orange oil (637mg) shown (^{1}H n.m.r.) to consist essentially of a single product.

Separation of the crude material on a Chromatotron equipped with a silica-gel PF-254 plate and eluting with petroleum ether/ether (90:10) gave pure 2-t-butyl-4,6-dimethyl-4-nitrocyclohexa-2,5-dienone (82) as pale-yellow crystals, m.p. (recrystallised from methanol) 67-68.5°(dec.)(lit.[33] 63-65°(dec.)); ν_{max}(nujol) 1678, C=O; 1655, 1623, cross-conjugated dienone; 1545 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.26, s, 9H, t-butyl; 1.86, s, 3H, C4-methyl; 1.94, bs, 3H, C6-methyl; 6.78, bs, 2H, H3, H5; λ_{max} (cyclohexane) 235 nm (ε 11550).

B. - A solution of the phenol (79)(1g) in benzene (10ml) was deoxygenated by a stream of pure nitrogen. A solution of nitrogen dioxide (520mg; 2 molar-equivalents) in benzene (1.3ml) was added over 30 min to the cooled (*c.* 5°), stirred solution of the phenol under an atmosphere of nitrogen. After the addition was complete, the benzene solvent was removed at 20° under reduced pressure to give a pale-orange oil (1418mg) shown (^{1}H n.m.r.) to consist essentially of a single product.

Separation of the crude mixture on a Chromatotron as for A.- and subsequent recrystallisation from methanol gave 2-t-butyl-4,6-dimethyl-4-nitrocyclohexa-2,5-dienone (82) identical in all respects to the material in A.-

Reaction of 2-t-butyl-4,6-dimethyl-4-nitrocyclohexa-2,5-dienone (82) with nitrogen dioxide in benzene

A solution of the nitrodienone (82)(418mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at $<10^{\circ}$ for 30s and stirring continued for 5h while the mixture was stored at 20° under an atmosphere of nitrogen dioxide. After 5h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a pale-yellow solid (587mg) shown (^{1}H n.m.r.) to be a mixture of the two trinitroketones (80) and (81) (*c.* 1:1).

Fractional crystallisation of the above crude mixture from dichloromethane/pentane, without heating, gave trinitroketone (80)(88mg), identical (i.r., ^{1}H n.m.r., m.p., m.m.p.) with an authentic sample. Removal of the solvent from the mother liquor of the above crystallisation under reduced pressure gave a residue which upon fractional crystallisation from dichloromethane/pentane gave trinitroketone (81)(17mg), identical (i.r., ^{1}H n.m.r., m.p., m.m.p.) with an authentic sample.

2,4-Di-t-butyl-6-chloromethylphenol

A solution of 2,4-di-t-butylphenol (20g), Formalin (30% w/v Formaldehyde in water; 20ml) and acetic acid (100ml) was placed in a 250ml three-neck round-bottom flask fitting with a reflux condenser, mechanical stirrer and a gas bubbler.[75] With the stirrer operating at a moderate stirring rate, dry Hydrogen chloride gas (generated by dehydration of concentrated hydrochloric acid with concentrated sulphuric acid and subsequent drying through concentrated sulphuric acid "scrubbing") was passed through the solution for 2h at room temperature. The solution was then poured into an ice (100g)/water (100ml) mixture, causing oiling of the product. The product was extracted into chloroform (200ml) and the chloroform extracts were washed free of acid (as judged by blue litmus), dried, and evaporated under reduced pressure to give a viscous pale-yellow liquid (24.32g; 98%) shown (^{1}H n.m.r.) to be essentially pure 2,4-di-t-butyl-6-chloromethylphenol (^{1}H n.m.r. (CCl_4) δ 1.30, s, 9H, t-butyl; 1.42, s, 9H, t-butyl; 4.60, s, 2H, CH_2Cl; 5.38, s, 1H, D_2O exch., OH; 6.97, d, 1H, $J_{3,5}$ 2.5Hz, H3; 7.25, d, 1H, $J_{5,3}$ 2.5Hz, H5).

2,4-Di-t-butyl-6-methylphenol (84)

To a solution of 2,4-di-t-butyl-6-chloromethylphenol (24g) in dry methanol (125ml) in a long-neck 250ml round-bottom flask was added palladium on charcoal (4g; 5% w/w) and the mixture agitated vigorously in a hydrogen atmosphere until one mole-equivalent of hydrogen was consumed. After filtration to remove the suspended material, the solvent was evaporated under reduced pressure to give a pale-yellow oil (19.2g; 92%) shown (^{1}H n.m.r.) to be essentially a pure compound.

Fractional distillation of the crude material at diminished

pressure gave pure 2,4-di-t-butyl-6-methylphenol (84) (11.8g) as a viscous pale-straw coloured liquid which rapidly solidified, m.p. 47-49° (lit.[63c] 51°); ν_{max}(nujol) 3625, OH; 1600 cm^{-1}, aromatic; ^1H n.m.r. (CCl_4) δ 1.28, s, 9H, C-4 t-butyl; 1.41, s, 9H, C-2 t-butyl; 2.18, s, 3H, methyl; 4.50, s, 1H, D_2O exch., OH; 6.86, d, 1H, $J_{5,3}$ 2.5Hz, H5; 7.07, d, 1H, $J_{3,5}$ 2.5Hz, H3.

Reaction of 2,4-di-t-butyl-6-methylphenol (84) with nitrogen dioxide in benzene

A solution of the phenol (84)(620mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10° for 30s and stirring continued for 5h while the mixture was stored at 20° under an atmosphere of nitrogen dioxide. The solution remained green in colour during the 5h period. After 5h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a viscous pale-yellow oil (1040mg) which gradually solidified, shown to be a mixture of (85),(86),(89),(87),(90),(91) and (88) (*c*. 39:30:7:14:4:3:3).

Separation of the crude mixture was achieved using a Chromatotron equipped with a Silica-gel PF-254 plate. Separated components were further purified by recrystallisation from either dichloromethane/light petroleum or ether/light petroleum mixtures.

Elution with petroleum ether/ether (80:20) gave 2,4-di-t-butyl-6-methyl-*r*-2,*t*-5,*c*-6-trinitrocyclohex-3-enone (85) as a colourless crystalline solid, m.p. 91-92°(dec.), (Found: C, 50.8; H, 6.7; N, 11.5. $C_{15}H_{23}N_3O_7$ requires C, 50.4, H, 6.5; N, 11.8%); ν_{max}(nujol) 1755, α,α'-dinitroketone; 1652, C=C; 1570 (br) cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.27, s, 9H, t-butyl;

1.29, s, 9H, t-butyl; 1.85, s, 3H, methyl; 6.17, s, 1H, H5; 6.78, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 18.92, methyl; 26.74, t-butyl methyls; 28.94, t-butyl methyls; 38.55, C-Me_3; 42.01, C-Me_3; 89.78, C2/C5/C6; 91.75, C5/C6/C2; 94.64, C6/C2/C5; 127.14; C3; 147.12, C4; 185.51, C1.

Elution with petroleum ether/ether (50:50) gave 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*t*-6-trinitrocyclohex-3-enone (86) as a colourless crystalline solid, m.p. 102-103°(dec.); ν_{max}(nujol) 1743, α,α'-dinitroketone; 1657, C=C; 1560 (br) cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.12, s, 9H, C-2 t-butyl; 1.30, s, 9H, C-4 t-butyl; 1.90, s, 3H, methyl; 6.07, bs, 1H, H5; 6.59, bs, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 21.38, methyl, 25.94, t-butyl methyls; 29.04, t-butyl methyls; 38.27, C-Me_3; 41.20, C-Me_3; 87.46, C2/C5/C6; 92.53, C5/C6/C2; 96.07, C6/C2/C5; 126.48, C3; 145.92, C4; 184.20, C1; the structure of trinitroketone (86) was determined by X-ray crystal structure analysis (See Appendix).

Elution with petroleum ether/ether (25:75) gave 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*c*-6-dinitrocyclohex-3-enone (89) as a colourless crystalline solid, m.p.103.5-104.5°; ν_{max}(nujol) 3575, OH; 1755, α-nitroketone; 1660, C=C; 1565-1550(br) cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.18, s, 9H, C-2 t-butyl; 1.24, s, 9H, C-4 t-butyl; 1.80, s, 3H, methyl; 2.32, s, 1H, D_2O exch., OH; 6.15, s, 1H, H5; 6.34, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3); not obtainable at -25°; the structure of hydroxydinitroketone (89) was determined by X-ray crystal structure analysis (See Appendix).

Elution with ether gave 2,4-di-t-butyl-6-methyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (87) as a colourless crystalline solid, m.p. 110-111°(dec.(dec.); ν_{max}(nujol) 1765, α,α'-dinitroketone; 1640, C=C; 1580, 1566, 1547 cm^{-1}, NO_2; ^1H n.m.r.

($CDCl_3$) δ 1.28, s, 9H, t-butyl; 1.32, s, 9H, t-butyl; 1.78, s, 3H, methyl; 5.86, bs, 1H, H5; 6.80, bs, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 19.61, methyl; 24.33, t-butyl methyls, 26.43, t-butyl methyls; 36.13, C-Me_3; 39.12, C-Me_3; 86.52, C2/C5/C6; 94.17, C5/C6/C2; 94.43, C6/C2/C5; 124.42, C3; 145.44, C4; 184.69, C1; the structure of trinitroketone (87) was determined by X-ray crystal structure analysis (See Appendix).

Further elution with ether gave 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*t*-6-dinitrocyclohex-3-enone (90) as a colourless crystalline solid, m.p. 134.5-135.5°(dec.); ν_{max}(nujol) 3570, OH; 1755, α-nitroketone; 1650, C=C; 1575, 1555 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.21, s, 9H, C-2 t-butyl; 1.28, s, 9H, C-4 t-butyl; 2.06, s, 3H, methyl; 2.60, s, 1H, D_2O exch., OH; 5.80, bs, 1H, H5; 6.31, bs, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3); not obtainable at -25°; the structure of hydroxydinitroketone (90) was determined by X-ray crystal structure analysis (See Appendix).

Elution with ether/methanol (90:10) gave 2,4-di-t-butyl-*c*-6-hydroxy-6-methyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (91) as a colourless crystalline solid, m.p. 131-133°(dec.); ν_{max}(nujol) 3500, OH; 1735, α-nitroketone; 1645, C=C, 1575, 1555 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.19, s, 9H, C-2 t-butyl, 1.27, s, 9H, C-4 t-butyl; 1.37, s, 3H, methyl; 4.06, s, 1H, D_2O exch., OH; 5.48, bs, 1H, H5; 6.57, bs, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3); not obtainable at -25°; the structure of hydroxydinitroketone (91) was determined by X-ray crystal structure analysis (See Appendix).

Elution with methanol gave 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (88) as a colourless crystalline solid, m.p. 132-133°(dec); ν_{max}(nujol) 1755, α,α'-dinitroketone; 1645, C=C; 1580, 1565, 1558 cm^{-1}, NO_2;

^{1}H n.m.r. ($CDCl_3$) δ 1.21, s, 9H, C-2 t-butyl, 1.30, s, 9H, C-4 t-butyl; 1.85, s, 3H, methyl; 5.84, bs, 1H, H5; 6.60, bs, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3); not obtainable at -25°; the structure of trinitroketone (88) was determined by X-ray crystal structure analysis (See Appendix).

2,4-Di-t-butyl-6-methyl-4-nitrocyclohexa-2,5-dienone (92)[33]

A. - Fuming nitric acid (0.11ml; d 1.5) was added dropwise to a stirred solution of 2,4-di-t-butyl-6-methylphenol (84)(500mg) in acetic acid (3ml) cooled in an ice-water bath. The solution was then extracted with light petroleum (2x10ml) and the light petroleum extracts washed free of acid with water (3x50ml), dried, and evaporated under reduced pressure to give a viscous yellow oil (577mg) which gradually solidified.

Separation of the crude material on a Chromatotron equipped with a Silica-gel PF-254 plate and elution with petroleum ether/ether (90:10) gave pure 2,4-di-t-butyl-6-methyl-4-nitrocyclohexa-2,5-dienone (92) as a pale-yellow crystalline solid, m.p. 62-63°(dec.) [lit.[33] 66-67°(dec.)]; ν_{max}(nujol) 1672, C=O; 1650, 1620, cross-conjugated dienone; 1542 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.10, s, 9H, C-2 t-butyl; 1.27, s, 9H, C-4 t-butyl; 1.95, d, 3H, $J_{CH_3,H5}$ 1.5Hz, methyl; 7.10, q, 1H, J_{H5,CH_3} 1.5Hz, H5; 7.14, s, 1H, H3; ^{13}C n.m.r. ($CDCl_3$); not obtainable; λ_{max}(cyclohexane) 240 nm (ε 10750) [lit.[33] λ_{max} 238 nm].

B. - A solution of the phenol (84)(500mg) in benzene (3ml) was deoxygenated by a stream of pure nitrogen. A solution of nitrogen dioxide (210mg; 2 molar-equivalents) in benzene (1ml) was added over 30 min to the cooled (*c.* 5°), stirred solution of the phenol under an atmosphere of nitrogen. After the addition was complete, the benzene solvent was removed at 20° under reduced pressure to give a pale-yellow solid (600mg) shown

(^{1}H n.m.r.), to consist essentially of a single product.

Separation of the crude material on a Chromatotron, as for A.- gave 2,4-di-t-butyl-6-methyl-4-nitrocyclohexa-2,5-dienone (92) identical to the material in A.-.

Reaction of 2,4-di-t-butyl-6-methyl-4-nitrocyclohexa-2,5-dienone (92) with nitrogen dioxide in benzene

A solution of the 4-nitrodienone (92)(520mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at $<10^{\circ}$ for 30s and stirring continued for 5h while the mixture was stored at 20° under an atmosphere of nitrogen dioxide. After 5h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a viscous pale-yellow oil (702mg) which gradually solidified, shown to be a mixture of (85),(86),(89),(87),(90), (91) and (88)(*c.* 44:30:8:8:4:3:3).

Separation of the crude mixture on a Chromatotron equipped with a Silica-gel PF-254 plate and subsequent recrystallisation from either dichloromethane/light petroleum or ether/light petroleum mixtures gave samples of (85),(86),(87),(88),(89), (90) and (91) identical in all respects (m.p., m.m.p., i.r., ^{1}H n.m.r.) with authentic materials.

Reaction of 2,6-di-t-butyl-4-methylphenol (62) with Nitrogen dioxide in cyclohexane[67]

(A) 10 min - A solution of the phenol (62)(500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10° for 30s and stirring continued for 10 min while the mixture was stored at 10° under an atmosphere of nitrogen dioxide. The solution was initially green in colour. After 10 min the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give a solid (567mg; 94%) identified as 2,6-di-t-butyl-4-methyl-4-nitrocyclohexa-2,5-dienone (64),[33,56] m.p. (recrystallised from Methanol) 97-98°(dec,), ν_{max}(nujol) 1670, C=O; 1650, 1628, cross-conjugated dienone; 1548 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.25, s, 18H, t-butyls; 1.84, s, 3H, methyl; 6.75, s, 2H, H3, H5; ^{13}C n.m.r. (CD_3COCD_3) δ 26.4, CH_3; 29.4, t-butyl methyls; 35.6, $\underline{C}Me_3$; 86.2, C4; 136.3, C3, C5; 149.5, C2, C6; 205.7, C1; λ_{max} (cyclohexane) 234 nm (ε 10850).

(b) 22h - Reaction of the phenol (62)(1g) in cyclohexane (10ml) as for (A), except that stirring of the reaction mixture under an atmosphere of nitrogen dioxide was continued for 22h, gave a precipitate (343mg), m.p. 114-115°(dec.), shown to be a mixture (*c.* 1:1) by ^1H n.m.r. ($CDCl_3/CD_3CN$, 3:1) δ 1.04, 1.24, 1.27, 1.31, 1.97, 2.11, 3.83, D_2O exch., 5.30, 5.58, 6.28, 6.70. Recrystallisation of the above mixture from dichloromethane/pentane, without heating, gave the pure 2,6-di-t-butyl-4-methyl-*r*-4,*c*-5,*c*-6-trinitrocyclohex-2-enone (95)(144mg), m.p. 118-118.5°(dec.), ν_{max}(nujol) 1700, conjugated C=O; 1630, C=C; 1580, 1568, 1558 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3/CD_3CN$, 3:1) δ 1.24, s, 9H, t-butyl; 1.31, s, 9H, t-butyl; 2.11, s, 3H, methyl; 5.58,

s, 1H, H5; 6.70, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3) δ 26.7, 27.8, 29.4, 36.9, 42.4, 84.3, 86.6, 136.9, 152.8, 206.2; λ_{max} ($CHCl_3$) 242 nm (ε 9700); the structure of the trinitroketone (95) was determined by X-ray crystal structure analysis[67] (See Appendix).

Removal of the solvent from the mother liquor of the above crystallisation under reduced pressure gave a residue which was dissolved in chloroform/acetonitrile (6:1) and stored at 20° for 16h. Removal of the solvent under reduced pressure gave a residue which upon crystallisation from dichloromethane/pentane gave pure 2,6-di-t-butyl-*c*-6-hydroxy-4-methyl-*r*-4,*c*-5-dinitrocyclohex-2-enone (96), m.p. 124-125°(dec.), ν_{max}(nujol) 3560, OH; 1695, conjugated C=O, 1572, 1565 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.04, s, 9H, t-butyl; 1.27, s, 9H, t-butyl; 1.97, s, 3H, methyl; 3.83, s, 1H, OH, D_2O exch.; 5.30, s, 1H, H5; 6.28, s, 1H, H3; ^{13}C n.m.r. (CD_3COCD_3, -25°) δ 22.9, 26.2, 29.3, 36.6, 41.3, 80.0, 85.7, 88.7, 133.5, 156.7, 197.4; λ_{max} ($CHCl_3$) 240 nm (ε 4800). Brunton *et.al.*[56] quote m.p. 124-126°(dec.), ν_{max}(medicinal white oil) 3540, 1695,1565 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 1.02, 9H; 1.24, 9H; 1.95, 3H; 3.82, 1H, D_2O exch.; 5.30, 1H; 6.28, 1H. The structure of the hydroxydinitroketone (96) was determined by X-ray crystal structure analysis.[67] (See Appendix).

Removal of solvent from the cyclohexane filtrate above, under reduced pressure, gave a residue (1004mg), shown by i.r., ^1H n.m.r. to be essentially pure 4-nitrodienone (64).

Reaction of 2,6-di-t-butyl-4-methylphenol (62) with nitrogen dioxide in benzene[67]

A solution of the phenol (62)(1g) in benzene (10ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10° for 30s, and stirring continued for a further 16h under an

atmosphere of nitrogen dioxide. The solution was initially green in colour. After 16h the excess nitrogen dioxide was removed in a stream of nitrogen and the material which had deposited was isolated by filtration and shown to be the trinitroketone (95)(203mg), m.p. 118-118.5°(dec.), identical (i.r. and ^{1}H n.m.r.) with authentic material.

Removal of the solvent from the filtrate under reduced pressure gave a residue (1287mg), shown (^{1}H n.m.r.) to consist mainly of the 4-nitrodienone (64), together with a small amount of the trinitroketone (95)(*c.* 10%). Although traces of the hydroxydinitroketone (96) were detected, the estimated yield was <1%.

Reaction of 2,6-di-t-butyl-4-methyl-4-nitrocyclohex-2,5-dienone (64) with nitrogen dioxide[67]

In cyclohexane solution. - A suspension of the 4-nitrodienone (64)[33,56](500mg) in cyclohexane (5ml) was deoxygenated by a stream of pure nitrogen. The suspension was cooled to *c.* 5° and pure nitrogen dioxide bubbled through it for 30s. The reaction mixture was then stirred at 20° under an atmosphere of nitrogen dioxide for 16h. Excess nitrogen dioxide was removed in a stream of nitrogen and the precipitated material was isolated by filtration and shown to be a mixture (127mg; *c.* 3:4)(^{1}H n.m.r.) of the hydroxydinitro-(96) and trinitro-(95) ketones.[67]

Removal of solvent from the filtrate under reduced pressure gave a residue (400mg), shown (i.r., ^{1}H n.m.r.) to be essentially pure 4-nitrodienone (64).

In benzene solution. - Reaction of the 4-nitrodienone (64) (500mg), as above except in benzene solution, gave precipitated material (105mg) shown to be pure trinitroketone (95), identical

(i.r., ^{1}H n.m.r.) with authentic material.

The filtrate yielded essentially pure 4-nitrodienone (64) (420mg) identical (i.r., ^{1}H n.m.r.) with authentic material.

2,6-Di-t-butyl-6-hydroxy-4-methylcyclohexa-2,4-dienone (97)[67]

To hot chloroform (25ml) was added the hydroxydinitroketone (96)(313mg) and the solution heated under reflux for 1.5h. Removal of the solvent under reduced pressure gave the crude 6-hydroxydienone (97)(227mg) as a dark red wax , ν_{max}(nujol) 3500, OH; 1665, C=O; 1570 cm^{-1}, homoannular linear dienone; ^{1}H n.m.r. ($CDCl_3$) δ 1.27, s, 18H, t-butyls; 2.13, d, 3H, $J_{Me,5}$ 1.5Hz, methyl; 6.15, m, 1H, $J_{5,Me}$ 1.5Hz, $J_{5,3}$ 2.5Hz, H5; 6.58, d, 1H, $J_{3,5}$ 2.5Hz, H3; λ_{max} ($CHCl_3$) 239, 400 nm (ε 3750, 1700). The above material was >90% 6-hydroxydienone (97) but attempts at its purification resulted in its decomposition. The material was stored at -78° prior to its reaction with nitrogen dioxide.

Reaction of 2,6-di-t-butyl-6-hydroxy-4-methylcyclohexa-2,4-dienone (97) with nitrogen dioxide in cyclohexane[67]

A suspension of the 6-hydroxydienone (97)(225mg) in cyclohexane (5ml) was deoxygenated with a stream of pure nitrogen. Nitrogen dioxide was bubbled through the stirred suspension for 30s, and the mixture was then stirred under an atmosphere of nitrogen dioxide for a further 16h. The excess nitrogen dioxide was removed in a stream of nitrogen, and the solvent evaporated under reduced pressure. The residue (302mg) was an orange oil shown by i.r., ^{1}H n.m.r. to be a complex mixture; no trace of the hydroxydinitroketone (96) could be detected in this mixture.

Some reactions of 2,6-di-t-butyl-4-methyl-*r*-4,*c*-5,*c*-6-trinitrocyclohex-2-enone (95)[67]

Attempted conversion into the hydroxydinitroketone (96).- A solution of the trinitroketone (95)(20mg) in dichloromethane (5ml) was shaken vigorously with water (2ml) for 5 min. The dichloromethane layer was separated and dried, and the solvent was removed under reduced pressure to give a residue (20mg), shown by i.r. and ^{1}H n.m.r. to be the pure trinitroketone (95).

Formation of 2,6-di-t-butyl-4-methyl-4-nitrocyclohexa-2,5-dienone (64) in chloroform/acetonitrile (6:1).- A solution of the trinitroketone (95)(100mg) in $CHCl_3/CH_3CN$ (7ml; 6:1) was stored at 20° for 16h. The solvents were removed under reduced pressure to give a residue (90mg), shown by ^{1}H n.m.r. to be a mixture (*c*. 2:1) of the 4-nitrodienone (64) and the trinitroketone (95).

Formation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (94) from 4-nitrodienone (64)

A suspension of the 4-nitrodienone (64)(1.5g) in a glacial acetic acid (20ml)/sodium acetate (anhydrous; 1.5g) solution was stirred vigorously, in the absence of light, for 168h. The solution was extracted with chloroform (4x25ml) and the chloroform layer was washed thoroughly with water, dried and the solvent removed under reduced pressure to give an orange residue (1.2g) shown by ^{1}H n.m.r. to be essentially a single pure compound. Purification by silica column chromatography gave pure 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (94), m.p. 110-111° (lit.[68] 113-114°); ν_{max}(nujol) 3300, OH; 1665, C=O; 1645, 1618, cross-conjugated dienone; ^{1}H n.m.r. ($CDCl_3$) δ 1.25, s, 18H, t-butyls; 1.42, s, 3H, methyl; 6.58, s, 2H, H3, H5;

^{13}C n.m.r. (CD_3COCD_3) δ 28.85, CH_3; 29.71; t-butyl CH_3's; 34.89, $\underline{C}Me_3$; 67.11, C4; 144.56, C2,C6; 145.73, C3,C5; 205.92, C1; λ_{max} ($CHCl_3$) 240 nm (ε 8300).

Reaction of 2,4,6-tri-t-butylphenol (98) with Nitrogen dioxide in benzene

(A) 2h. - A solution of the phenol (98)(500mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at $<10^{o}$ for 30s and stirring continued for 2h while the mixture was stored at 20^{o} under an atmosphere of nitrogen dioxide. The solution remained green in colour during the 2h period. After 2h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give an orange solid (585mg; 100%) identified as 2,4,6-tri-t-butyl-4-nitro-cyclohexa-2,5-dienone (99), m.p. (recrystallised from methanol) $83.5-84^{o}$(dec.)(lit.[33,55] $83.5-84^{o}$(dec.)), ν_{max}(nujol) 1670, C=O; 1650, 1620, cross-conjugated dienone; 1550 cm^{-1}, NO_2; ^{1}H n.m.r. ($CDCl_3$) δ 1.07, s, 9H, C4 t-butyl; 1.27, s, 18H, C2,C6 t-butyl's; 7.12, s, 2H, H3, H5; ^{13}C n.m.r. (CD_3COCD_3) δ 26.32, C4 t-butyl methyls; 29.53, C2,C6 t-butyl methyls; 36.06, C2,C6 $\underline{C}Me_3$'s; 42.35, C4 $\underline{C}Me_3$; 134.39, C3,C5; 150.19, C2,C6; 205.75, C1; λ_{max}(cyclohexane) 241 nm (ε 10600).

(B) 23h. - Reaction of the phenol (98)(500mg) in benzene (5ml) as for (A), except that stirring of the reaction mixture under an atmosphere of nitrogen dioxide was continued for 23h. After 23h the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent was removed under reduced pressure to give an orange oil (612mg), shown (i.r., ^{1}H n.m.r.) to be a mixture of (99),(100) and (101)(*c.* 1:8:1).

Separation of the crude mixture was achieved using a Chromatotron equipped with a Silica-gel PF-254 plate.

Elution with petroleum ether/ether (95:5) gave pure 4-nitrodienone (99), identical (i.r., ^{1}H n.m.r., m.p., m.m.p.)

with authentic material.

Elution with petroleum ether/ether (90:10) gave pure 2,6-di-t-butylbenzo-1,4-quinone (100) as a pale-yellow solid, m.p. (recrystallised from methanol) 65-66° (lit.[69] 68°); ν_{max} (nujol) 1670, 1660, [1,4]quinone; 1600 cm^{-1}, C=C; ^1H n.m.r. (CCl_4) δ 1.30, s, 18H, t-butyls; 6.42, s, 2H, H3, H5; λ_{max} (methanol) 254 nm (ε 10600).

Elution with petroleum ether/ether (80:20) gave pure 2-t-butyl-4,6-dinitrophenol (101) as a pale-yellow solid, m.p. (recrystallised from methanol) 126-127° (lit.[70] 125-126°); ν_{max} (nujol) 3400(br), OH; 1610, C6-nitro; 1560 cm^{-1}, C4-nitro; ^1H n.m.r. ($CDCl_3$) δ 1.51, s, 9H, t-butyl; 8.47, d, 1H, $J_{3,5}$ 3Hz, H3; 8.96, d, 1H, $J_{5,3}$ 3Hz, H5; λ_{max} (methanol) 212 nm (ε 12300); 263 nm (ε 10900); 366 nm (ε 6400); (Found: M^+(CI), 240. Calculated for $C_{10}H_{12}N_2O_5$: M^+, 240).

Reaction of 2,6-di-t-butyl-4-nitrophenol (102) with nitrogen dioxide in benzene

A suspension of the phenol (102)(500mg) in benzene (5ml) was deoxygenated by a stream of pure nitrogen. Pure nitrogen dioxide was bubbled through the stirred solution at <10° for 30s and stirring continued for 10 min while the mixture was stored at *c.* 5° under an atmosphere of nitrogen dioxide. During this time the solution became a deep orange-brown colour and effervesced strongly. After 10 min the excess nitrogen dioxide was removed in a stream of nitrogen and the solvent removed under reduced pressure to give an orange solid identified as 2-t-butyl-4,6-dinitrophenol (101), identical in all respects (i.r., u.v., ^1H n.m.r., m.p., m.m.p.) with an authentic sample.[70]

6.5 EXPERIMENTAL SECTION RELATING TO CHAPTER 5

4-t-Butyl-*r*-2-(4'-t-butyl-2',6'-dimethylphenoxy)-*t*-6-hydroxy-2,6-dimethyl-*t*-5-nitrocyclohex-3-enone (109)[71]

A solution of 4-t-butyl-2,6-dimethylphenol (66)(2g) in benzene (12ml) was deoxygenated by a stream of pure nitrogen. A solution of nitrogen dioxide (520mg; 1 molar-equivalent) in benzene (5.6ml) was added over 30 min to the cooled (*c*. 5°), stirred solution of the phenol under an atmosphere of nitrogen. After the addition was complete, the benzene solvent was removed at 20° under reduced pressure (time elapsed *c*. 30 min) to give an oily residue (2.4g). Addition of pentane to this oily residue gave the hydroxynitrophenoxyketone (109)(615mg), m.p. 122.5-123°(dec.); ν_{max}(nujol) 3460, OH; 1730, C=O; 1645, C=C; 1562 cm^{-1}, NO_2; ^1H n.m.r. ($CDCl_3$) δ 1.22, s, 9H, t-butyl; 1.29, s, 9H, t-butyl; 1.43, s, 3H, C-6 methyl; 1.71, s, 3H, C-2 methyl; 2.23, s, 6H, aryl methyls; 4.20, s, 1H, D_2O exch., OH; 5.58, d, 1H, $J_{5,3}$ 1.5Hz, H5; 6.47, d, 1H, $J_{3,5}$ 1.5Hz, H3; 7.01, br s, 2H, aryl protons; ^{13}C n.m.r. ($CDCl_3$) (Carbon designations as in Fig.20) δ 18.94, C7; 19.09, C19, C21; 23.85, C9; 28.61, C10, C11,C12; 31.42, C22,C23,C24; 34.10, C20; 36.48; C8; 75.42, C6/C2; 78.84, C2/C6; 94.83, C5; 126.11, C15,C17; 132.48, C14,C18; 134.07, C3; 139.76, C4; 147.31, C16/C13; 148.91, C13/C16; 204.33, C1; the structure of the hydroxynitrophenoxyketone (109) was determined by X-ray crystal structure analysis. (See Appendix).

The residue from the above crystallisation was an oil (*c*. 1.7g), the ^1H n.m.r. spectrum of which indicated the presence of further compound (109) (*c*. 240mg). No further components could be isolated from this unstable mixture.

^{1}H n.m.r. Study of the Formation of Compound (109)[71]

Nitrogen dioxide (1 molar-equivalent) was added to the phenol (66)(500mg), as above. After completion of the addition, the ^{1}H n.m.r. spectrum of the resulting solution was monitored for 24h. Initially the spectrum obtained was consistent with the presence of a mixture (*c.* 1:1) of the phenol (66) and the 4-nitrodienone (77).[64] During the 24h period the ^{1}H n.m.r. spectrum of the solution became more complex, and at the end of the period revealed the presence of the hydroxynitrophenoxyketone (109)(*c.* 30% yield). The final spectrum was essentially identical with that of the crude product from the preparative reaction.

^{1}H n.m.r. Study of 4-nitrodienone (77) in Benzene Solution

The ^{1}H n.m.r. spectrum of a solution of the 4-nitrodienone (77)[64] in benzene was monitored for 24h. During that period the ^{1}H n.m.r. spectrum of the solution became complex, but no signals associated with the hydroxynitrophenoxyketone (109) were detected.

^{1}H n.m.r. Study of a Mixture of 4-nitrodienone (77) and Phenol (66) in Benzene Solution

The ^{1}H n.m.r. spectrum of an equimolar solution of the 4-nitrodienone (77)[64] and the phenol (66) in benzene was monitored for 24h. During the 24h period the ^{1}H n.m.r. spectrum of the solution became complex, but no signals associated with the hydroxynitrophenoxyketone (109) were detected.

Addition of Two Molar Equivalents of Nitrogen Dioxide to 4-t-butyl-2,6-dimethylphenol (66) in Benzene Solution, Followed by the Addition of Phenol (66)(1 mole)

Nitrogen dioxide (2 molar-equivalents) was added to the

phenol (66)(500mg), as above. After the completion of the addition the ^{1}H n.m.r. spectrum of the solution revealed the presence of the 4-nitrodienone (77) as the sole organic product. This benzene solution was investigated in three ways:

a) The ^{1}H n.m.r. spectrum of the solution was monitored for 24h. No evidence for the formation of the hydroxynitrophenoxyketone (109) was obtained.

b) An aliquot of the benzene solution was extracted with water; the aqueous extract gave a positive test for nitrous acid (Griess-Ilosvay test[72])

c) 4-t-butyl-2,6-dimethylphenol (66)(1 molar-equivalent) was added to the original benzene solution and the ^{1}H n.m.r. spectrum of the mixture monitored for 24h. The hydroxynitrophenoxyketone (109) was formed in *c*. 25% yield.

APPENDIX

The data sets used for the X-ray crystal structure analyses contained in this thesis were obtained on two different instruments. For the dichlorodinitrocyclopentenol derivative (44) and the dichlorodinitrocyclohex-3-enone (54)(Chapter 2), crystal data, established from precession photographs and measured accurately, by using a Hilger & Watts four-circle diffractometer, are presented below. Ni-filtered Cu Kα X-radiation [λ(Cu Kᾱ) 1.5418 Å] and the θ/2θ scan technique were used to collect reflection intensities out to a Bragg angle θ, given below. The space group was, in each case, determined unambiguously as a result of the structure analyses reported below but initially indicated by systematic absences of appropriate reflections. The cell parameters were determined, in each case, by least-squares refinement, the setting angles of 25 accurately centred reflections ($40^{o}<2\theta<65^{o}$) being used. Absorption corrections were essential to obtain correct relative intensities.

Crystal data for 1-acetyl-3,t-5-dichloro-2,4-dimethyl-t-2,5-dinitrocyclopent-3-en-r-1-ol (44).[43] - $C_9H_{10}Cl_2N_2O_6$, M 313.1, monoclinic, space-group $P2_1/n$, *a* 9.797(1), *b* 10.170(1), *c* 13.175(1) Å, β 97.78(2)°, *U* 1301 $Å^3$, D_m 1.52 gcm^{-3}, D_c 1.52 gcm^{-3}, *Z* 4, μ(Cu Kᾱ) 45.78 cm^{-1}. The crystal was colourless and of approximate dimensions 0.88 by 0.65 by 0.09 mm. Number of independent reflections measured 1666, number with $I>3\sigma(I)$ 1443; maximum Bragg angle θ, 57°; *g* 0.00721; *R*-factor 0.0492 (for 1441 reflections; reflections $\bar{1}11$ and 002 suffered from low-angle extinction as judged by anomalously low $|F_o|$ relative to $|F_c|$ and were omitted from the final least-squares analysis);

WR 0.0632; absorption corrections, maximum 5.763, minimum 1.403.

Crystal data for 3,t-5-dichloro-t-6-hydroxy-2,4,6-trimethyl-r-2,5-dinitrocyclohex-3-enone (54).[45] - $C_9H_{10}Cl_2N_2O_6$, M 313.1, monoclinic, space-group $P2_1/c$, *a* 6.129(2), *b* 25.869(5), *c* 8.122(2) Å, β 106.45(3)°, *U* 1235 Å^3, *Dm* 1.68 gcm^{-3}, *Dc* 1.68 gcm^{-3}, *z* 4, μ(Cu Kᾱ) 48.21 cm^{-1}. The crystal was colourless and of approximate dimensions 0.8 by 0.34 by 0.35 mm. Number of independent reflections measured 1582, number with $I>3\sigma(I)$ 1268; maximum Bragg angle θ, 57°; *g* 0.0012; *R*-factor 0.078; *WR* 0.075; absorption corrections, maximum 4.98, minimum 1.78.

Intensity data were processed by means of a Burroughs B6930 computer and programs HILGOUT (based on DRED by J.F. Blount and PICKOUT by R.J. Doedens) and ABSORB (a major revision, by L.K. and D. Templeton, of the program AGNOST installed on local Burroughs hardware by A. Zalkin). Structure solution and refinement (full-matrix least-squares) and geometry calculations were carried out on a Prime 750 computer by programs SHELX (G. Sheldrick) and GEOM (S. Motherwell). Diagrams were produced using ORTEP II (C.K. Johnson).

For the remaining 15 compounds whose structures were determined by X-ray crystal structure analysis (compounds (71), (72),(73),(74),(80),(81),(86),(87),(88),(89),(90),(91),(95),(96) and (109); Chapters 4 and 5), crystal data, established from precession photographs and measured accurately, by using a Nicolet XRD P3 four-circle diffractometer, are presented below. Molybdenum X-radiation [λ(Mo Kᾱ) 0.71069 Å] from a graphite crystal monochromator and either the θ/2θ or ω scan technique were used to collect reflection intensities out to a Bragg angle θ, given below. The space group was, in each case,

determined unambiguously as a result of the structure analyses reported below but initially indicated by systematic absences of appropriate reflections. The cell parameters were determined, in each case, by least-squares refinement, the setting angles of 25 accurately centred reflections ($20^{\circ}<2\theta<30^{\circ}$) being used. Absorption corrections were neither warranted nor applied.

Crystal data for 4-t-butyl-2,6-dimethyl-r-2,c-5,t-6-trinitrocyclohex-3-enone (71).[64] - $C_{12}H_{17}N_3O_7$, M 315.17, monoclinic, space-group $P2_1/c$, *a* 6.846(1), *b* 13.335(2), *c* 16.612(3) Å, β 94.06(2)°, *U* 1513 Å^3, *Dm* 1.38 gcm^{-3}, *Dc* 1.38 gcm^{-3}, *Z* 4, μ(Mo K$\bar{\alpha}$) 1.08 cm^{-1}. The crystal was colourless and of approximate dimensions 0.65 by 0.19 by 0.10 mm. θ/2θ scans; number of independent reflections measured 2123, number with $I>2.5\sigma(I)$ 1228; maximum Bragg angle θ, 23°; *g* 0.00024; *R*-factor 0.048 (for 1227 reflections; reflection 002 suffered from low-angle extinction and was omitted from the final least-squares analysis); *WR* 0.047.

Crystal data for 4-t-butyl-2,6-dimethyl-r-2,t-5,t-6-trinitrocyclohex-3-enone (72).[64] - $C_{12}H_{17}N_3O_7$, M 315.17, monoclinic, space-group $P2_1/n$, *a* 7.338(1), *b* 12.777(2), *c* 16.379(3) Å, β 100.46(1)°, *U* 1510 Å^3, *Dm* 1.40 gcm^{-3}, *Dc* 1.39 gcm^{-3}, *Z* 4, μ(Mo K$\bar{\alpha}$) 1.08 cm^{-1}. The crystal was colourless and of approximate dimensions 0.56 by 0.23 by 0.14 mm. θ/2θ scans; number of independent reflections measured 1973, number with $I>3\sigma(I)$ 1265; maximum Bragg angle θ, 22°; *R*-factor 0.042 (unit weights).

Crystal data for 4-t-butyl-2,6-dimethyl-r-2,c-5,c-6-trinitrocyclohex-3-enone (73).[64] - $C_{12}H_{17}N_3O_7$, M 315.17, orthorhombic, space-group $P2_12_12_1$, *a* 8.545(2), *b* 9.655(2),

c 18.185(3) Å, *U* 1500 Å^3, *Dm* 1.40 gcm^{-3}, *Dc* 1.40 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 1.09 cm^{-1}. The crystal was colourless and of approximate dimensions 0.65 by 0.44 by 0.29 mm. θ/2θ scans; number of independent reflections measured 2304, number with $I>3\sigma(I)$ 1947; maximum Bragg angle θ, 29°; *g* 0.0005; *R*-factor 0.045 (for 1946 reflections; reflection 011 suffered from low-angle extinction and was omitted from the final least-squares analysis); *WR* 0.051.

Crystal data for 4-t-butyl-c-6-hydroxy-2,6-dimethyl-r-2,c-5-dinitrocyclohex-3-enone (74).[64] - $C_{12}H_{18}N_2O_6$, M 286.16, monoclinic, space-group $P2_1/n$, *a* 6.677(1), *b* 12.956(2), *c* 17.185(3) Å, β 95.46(1)°, *U* 1480 Å^3, *Dm* 1.28 gcm^{-3}, *Dc* 1.28 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 0.97 cm^{-1}. The crystal was colourless and of approximate dimensions 0.69 by 0.16 by 0.11 mm. θ/2θ scans; number of independent reflections measured 2312, number with $I>3\sigma(I)$ 1129; maximum Bragg angle θ, 24°; *g* 0.001 (fixed); *R*-factor 0.052 (for 1126 reflections; reflections 002, 020 and 111 suffered from low-angle extinction and were omitted from the least-squares analysis); *WR* 0.054.

Crystal data for 2-t-butyl-4,6-dimethyl-r-4,c-5,t-6-trinitrocyclohex-2-enone (80). - $C_{12}H_{17}N_3O_7$, M 315.17, orthorhombic, space-group $Pna2_1$, *a* 17.642(7), *b* 13.806(4), *c* 6.074(1) Å, *U* 1479 Å^3, *Dm* 1.42 gcm^{-3}, *Dc* 1.42 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 1.10 cm^{-1}. The crystal was colourless and of approximate dimensions 0.63 by 0.11 by 0.09 mm. θ/2θ scans; number of independent reflections measured 1442, number with $I>2\sigma(I)$ 934; maximum Bragg angle θ, 25°; *g* 0.0004; *R*-factor 0.058; *WR* 0.044.

Crystal data for 2-t-butyl-4,6-dimethyl-r-4,t-5,c-6-trinitrocyclohex-2-enone (81). - $C_{12}H_{17}N_3O_7$, M 315.17, monoclinic,

space-group $P2_1/n$, a 13.716(3), b 6.137(2), c 18.731(4) Å, β 110.59(2)°, U 1476 Å^3, Dm 1.41 gcm^{-3}, Dc 1.42 gcm^{-3}, Z 4, μ(Mo K$\bar{\alpha}$) 1.10 cm^{-1}. The crystal was colourless and of approximate dimensions 0.63 by 0.20 by 0.09 mm. θ/2θ scans; number of independent reflections measured 1953, number with $I>2.5\sigma(I)$ 1264; maximum Bragg angle θ, 22°; g 0.00031; R-factor 0.049; WR 0.048.

Crystal data for 2,4-di-t-butyl-6-methyl-r-2,c-5,t-6-trinitrocyclohex-3-enone (86). - $C_{15}H_{23}N_3O_7$, M 357.03, orthorhombic, space-group $Pbca$, a 13.870(2), b 25.012(3), c 10.564(3) Å, U 3665 Å^3, Dm 1.29 gcm^{-3}, Dc 1.28 gcm^{-3}, Z 8, μ(Mo K$\bar{\alpha}$) 1.20 cm^{-1}. The crystal was colourless and of approximate dimensions 0.88 by 0.50 by 0.44 mm. ω scans; number of independent reflections measured 2541, number with $I>3\sigma(I)$ 1082; maximum Bragg angle θ, 23°; g 0.00044; R-factor 0.068 (for 1081 reflections; reflection 200 suffered from low-angle extinction and was omitted from the final least-squares analysis); WR 0.072.

Crystal data for 2,4-di-t-butyl-6-methyl-r-2,t-5,t-6-trinitrocyclohex-3-enone (87). - $C_{15}H_{23}N_3O_7$, M 357.03, monoclinic, space group $P2_1/c$, a 17.259(3), b 12.659(2), c 18.269(3) Å, β 115.84(1)°, U 3592 Å^3, Dm 1.31 gcm^{-3}, Dc 1.32 gcm^{-3}, Z 8, μ(Mo K$\bar{\alpha}$) 0.99 cm^{-1}. The crystal was colourless and of approximate dimensions 0.75 by 0.41 by 0.08 mm. ω scans; number of independent reflections measured 4902, number with $I>2.5\sigma(I)$ 2500; maximum Bragg angle θ, 23°; g 0.00022; R-factor 0.0604 (for 2499 reflections; reflection $\bar{2}02$ suffered from low-angle extinction and was omitted from the final least-squares analysis); WR 0.0563.

The structure consists of two, well separated, crystallographically independent molecules. The shortest intermolecular distances were between O(1) and H(24A) (2.63Å) and O(51) and H(28A)(2.70Å). Superposition of the two independent molecules, using the SHELXTL[76] program XFIT, revealed no gross differences of any chemical significance between the two molecules. The greatest deviation between the two structures is in the orientations of the 4-t-butyl groups which are staggered at approximately 30° to one another.

Crystal data for 2,4-di-t-butyl-6-methyl-r-2,c-5,c-6-trinitrocyclohex-3-enone (88). - $C_{15}H_{23}N_3O_7$, M 357.03, orthorhombic, space-group *Pbca*, *a* 14.459(3), *b* 12.461(2), *c* 19.863(4) Å, *U* 3579 Å^3, *D*m 1.33 gcm^{-3}, *D*c 1.32 gcm^{-3}, *Z* 8, μ(Mo Kᾱ) 0.99 cm^{-1}. The crystal was colourless and of approximate dimensions 0.69 by 0.44 by 0.35 mm. ω scans; number of independent reflections measured 2448, number with $I>3\sigma(I)$ 1100; maximum Bragg angle θ, 23°; *g* 0.00127; *R*-factor 0.0463 (for 1099 reflections; reflection 102 suffered from low-angle extinction and was omitted from the final least-squares analysis); *WR* 0.0505.

Crystal data for 2,4-di-t-butyl-r-2-hydroxy-6-methyl-t-5,c-6-dinitrocyclohex-3-enone (89). - $C_{15}H_{24}N_2O_6$, M 328.02, monoclinic, space group $P2_1/c$, *a* 9.528(3), *b* 21.472(7), *c* 9.517(3) Å, β 116.79(2)°, *U* 1738 Å^3, *D*m 1.25 gcm^{-3}, *D*c 1.25 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 0.91 cm^{-1}. The crystal was colourless and of approximate dimensions 0.51 by 0.43 by 0.48 mm. ω scans; number of independent reflections measured 2243, number with $I>3\sigma(I)$ 1097; maximum Bragg angle θ, 23°; *g* 0.00129; *R*-factor 0.0456 (for 1095 reflections; reflections 021 and 040 suffered from low-angle extinction and were omitted from the final

least-squares analysis); *WR* 0.049.

Crystal data for 2,4-di-t-butyl-r-2-hydroxy-6-methyl-t-5,t-6-dinitrocyclohex-3-enone (90). - $C_{15}H_{24}N_2O_6$, M 328.02 monoclinic, space-group $P2_1/n$, *a* 13.585(5), *b* 7.534(2), *c* 16.664(4) Å, β 92.45(3)°, *U* 1704 Å^3, *Dm* 1.29 gcm^{-3}, *Dc* 1.28 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 1.00 cm^{-1}. The crystal was colourless and of approximate dimensions 0.61 by 0.50 by 0.25 mm. ω scans; number of independent reflections measured 1833, number with $I>3\sigma(I)$ 1173; maximum Bragg angle θ, 21°; *g* 0.00072; *R*-factor 0.0484; *WR* 0.0531.

Crystal data for 2,4-di-t-butyl-c-6-hydroxy-6-methyl-r-2,c-5-dinitrocyclohex-3-enone (91). - $C_{15}H_{24}N_2O_6$, M 328.02, orthorhombic, space-group *Pbca*, *a* 13.642(2), *b* 13.567(2), *c* 18.125(3) Å, *U* 3355 Å^3, *Dm* 1.30 gcm^{-3}, *Dc* 1.29 gcm^{-3}, *Z* 8, μ(Mo Kᾱ) 0.94 cm^{-1}. The crystal was colourless and of approximate dimensions 0.94 by 0.22 by 0.19 mm. ω scans; number of independent reflections measured 1799, number with $I>2\sigma(I)$ 1316; maximum Bragg angle θ, 21°; *g* 0.00015; *R*-factor 0.0466 (for 1315 reflections; reflection 020 suffered from low-angle extinction and was omitted from the final least-squares analysis); *WR* 0.0440.

Crystal data for 2,6-di-t-butyl-4-methyl-r-4,c-5,c-6-trinitrocyclohex-2-enone (95). - $C_{15}H_{23}N_3O_7$, M 357.03, monoclinic, space-group $P2_1/n$, *a* 6.385(2), *b* 20.217(8), *c* 13.898(6) Å, β 95.30(3)°, *U* 1786 Å^3, *Dm* 1.32 gcm^{-3}, *Dc* 1.33 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 1.14 cm^{-1}. The crystal was colourless and of approximate dimensions 0.50 by 0.21 by 0.15 mm. θ/2θ scans; number of independent reflections measured 2337, number

with $I>3\sigma(I)$ 969; maximum Bragg angle θ, 22°; *g* 0.00001; *R*-factor 0.051; *WR* 0.037.

Crystal data for 2,6-di-t-butyl-c-6-hydroxy-4-methyl-r-4,c-5-dinitrocyclohex-2-enone (96). - $C_{15}H_{24}N_2O_6$, M 328.02, orthorhombic, space-group $P2_12_12_1$, *a* 15.708(8), *b* 16.692(8), *c* 6.424(3) Å, *U* 1684 Å^3, *Dm* 1.28 gcm^{-3}, *Dc* 1.29 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 1.08 cm^{-1}. The crystal was colourless and of approximate dimensions 0.30 by 0.26 by 0.15 mm. θ/2θ scans; number of independent reflections measured 1310, number with $I>2\sigma(I)$ 731; maximum Bragg angle θ, 22°; *g* 0.00183; *R*-factor 0.0598; *WR* 0.0582.

Crystal data for 4-t-butyl-r-2-(4'-t-butyl-2',6'-dimethylphenoxy)-t-6-hydroxy-2,6-dimethyl-t-5-nitrocyclohex-3-enone (109). - $C_{24}H_{35}NO_5$, M 417.55, monoclinic, space-group $P2_1/c$, *a* 12.277(2), *b* 9.683(3), *c* 20.196(5) Å, β 93.92(2)°, *U* 2395 Å^3, *Dm* 1.16 gcm^{-3}, *Dc* 1.16 gcm^{-3}, *Z* 4, μ(Mo Kᾱ) 0.87 cm^{-1}. The crystal was colourless and of approximate dimensions 0.55 by 0.51 by 0.37 mm. θ/2θ scans; number of independent reflections measured 3706, number with $I>3\sigma(I)$ 1764; maximum Bragg angle θ, 24°; *g* 0.00014; *R*-factor 0.061 (for 1763 reflections; reflection 100 suffered from low-angle extinction and was omitted from the final least-squares analysis); *WR* 0.055.

Intensity data were processed and structure solution and refinement (blocked-cascade least-squares) and geometry calculations were carried out using a Data General Nova 4X computer and the SHELXTL[76] (G. Sheldrick) system of programs (designed specifically for minicomputer use). Diagrams were produced using the SHELXTL graphics program XP and a Tektronix

4113A colour graphics unit and Tektronix 4662 plotter.

All of the structures determined in this present work were solved by using direct-methods and difference Fourier syntheses. Least-squares refinements were employed by using reflection weights $1/\sigma^2(F)+g(F^2)$. The function minimised was $\Sigma w(|F_O|-|F_C|)^2$. Anomalous dispersion corrections were from Cromer and Libermann.[77] Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms and all non-hydrogen atoms were assigned anisotropic thermal parameters, except in the cases of compounds (80) and (109) where the alicyclic ring carbon atoms retain isotropic thermal parameters. Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors other than those noted which were attributable to extinction.

Further, more comprehensive material regarding the structural information for the abovementioned structures (temperature factors, structure factor amplitudes, interatomic distances, bond angles and torsional angles) is deposited with the Editor-in-Chief, Editorial and Publications Service, CSIRO, 314 Albert Street, East Melbourne, Victoria 3002, Australia.

TABLE 1. Fractional coordinates for non-constrained atoms in 1-acetyl-3,*t*-5-dichloro-2,4-dimethyl-*t*-2,5-dinitrocyclopent-3-en-*r*-1-ol (44), $C_9H_{10}Cl_2N_2O_6$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U*
Cl(3)	4260(1)	423(1)	1117(1)	69(1)
Cl(5)	7564(1)	4157(1)	2860(1)	42(1)
C(1)	4951(3)	3311(3)	3248(3)	36(2)
C(2)	4088(3)	2115(3)	2761(3)	34(2)
C(3)	4818(3)	1737(3)	1885(3)	40(2)
C(4)	5767(4)	2551(4)	1672(3)	54(2)
C(5)	5863(4)	3676(4)	2399(3)	38(2)
C(6)	5912(4)	2972(4)	4266(3)	48(2)
C(7)	6878(4)	1829(4)	4344(3)	52(2)
C(8)	2554(3)	2429(4)	2437(4)	32(2)
C(9)	6601(5)	2500(6)	792(4)	90(4)
N(2)	4100(3)	1017(3)	3560(2)	45(2)
N(5)	5164(4)	4908(4)	1810(3)	57(2)
O(1)	4098(3)	4350(4)	3433(2)	49(2)
O(21)	3686(4)	1300(4)	4355(2)	87(2)
O(22)	4504(4)	-74(3)	3365(3)	94(2)
O(51)	4186(4)	4675(4)	1166(3)	78(3)
O(52)	5604(4)	5978(3)	2046(4)	77(2)
O(6)	5814(4)	3699(3)	4980(2)	88(2)
HO(6)	4440(60)	4530(60)	4030(50)	80(20)

* For anisotropic atoms, the equivalent isotropic temperature factor (U) is defined as one-third of the trace of the orthogonalised U_{11} tensor.

TABLE 2. Fractional coordinates for non-hydrogen atoms in 3,*t*-5-dichloro-*t*-6-hydroxy-2,4,6-trimethyl-*r*-2,5-dinitrocyclohex-3-enone (54), $C_9H_{10}Cl_2N_2O_6$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
Cl(3)	1129(3)	4205(1)	-1813(2)	52(1)
Cl(5)	5181(4)	4292(1)	4839(2)	107(2)
C(1)	5580(10)	3210(2)	1323(6)	33(3)
C(2)	3580(10)	3396(2)	-163(6)	31(3)
C(3)	3050(10)	3960(2)	19(7)	26(3)
C(4)	3890(10)	4255(2)	1390(7)	34(3)
C(5)	5620(10)	4048(2)	2942(7)	45(3)
C(6)	5770(10)	3440(2)	3091(6)	33(3)
C(7)	7950(10)	3266(2)	4417(7)	48(4)
C(8)	1510(10)	3037(2)	-378(7)	35(3)
C(9)	3260(10)	4829(2)	1442(8)	49(4)
N(2)	4430(10)	3357(2)	-1771(6)	52(3)
N(5)	7990(10)	4245(2)	2808(8)	42(3)
O(1)	6804(7)	2875(2)	1096(5)	46(3)
O(21)	6050(10)	3623(2)	-1792(5)	64(3)
O(22)	3470(10)	3074(2)	-2931(6)	91(4)
O(51)	8520(10)	4069(2)	1625(6)	47(3)
O(52)	9010(10)	4551(2)	3871(9)	75(4)
O(6)	3794(6)	3264(2)	3479(5)	38(2)

TABLE 3. Fractional coordinates for non-constrained atoms in 4-t-butyl-2,6-dimethyl-*r*-2,*c*-5,*t*-6-trinitrocyclohex-3-enone (71), $C_{12}H_{17}N_3O_7$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	2239(5)	378(3)	8977(2)	43(1)
C(2)	3025(5)	1354(3)	8626(2)	38(1)
C(3)	3202(5)	1299(2)	7730(2)	39(1)
C(4)	2291(5)	658(2)	7220(2)	34(1)
C(5)	971(5)	- 111(2)	7559(2)	38(1)
C(6)	1698(5)	- 485(3)	8399(2)	42(1)
C(7)	4928(6)	1658(3)	9095(2)	59(2)
C(8)	2489(5)	662(3)	6313(2)	41(1)
C(9)	380(7)	-1252(3)	8759(2)	68(2)
C(10)	3252(6)	- 354(3)	6036(2)	59(2)
C(11)	3881(6)	1475(3)	6067(2)	63(2)
C(12)	459(6)	849(3)	5889(2)	63(2)
N(2)	1563(5)	2212(2)	8786(2)	59(1)
N(5)	-1077(4)	304(2)	7639(2)	58(1)
N(6)	3631(5)	-1029(2)	8264(2)	54(1)
O(1)	2134(4)	273(2)	9693(2)	66(1)
O(21)	895(5)	2266(3)	9432(2)	104(2)
O(22)	1241(6)	2812(2)	8261(2)	119(2)
O(51)	-2415(4)	- 32(3)	7237(2)	106(2)
O(52)	-1238(4)	952(3)	8132(2)	105(2)
O(61)	3604(5)	-1666(2)	7747(2)	87(1)
O(62)	5071(5)	- 799(2)	8689(2)	81(1)
H(3)	4030(30)	1740(20)	7550(10)	13(7)
H(5)	810(40)	- 640(20)	7230(20)	14(8)

TABLE 4. Fractional coordinated for non-constrained atoms in 4-t-butyl-2,6-dimethyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (72), $C_{12}H_{17}N_3O_7$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	5789(5)	1714(3)	6254(2)	40(1)
C(2)	4569(5)	866(3)	6542(2)	35(1)
C(3)	4370(5)	957(3)	7439(2)	36(1)
C(4)	4987(5)	1729(3)	7951(2)	33(1)
C(5)	5928(5)	2655(3)	7614(2)	34(1)
C(6)	7060(5)	2295(3)	6967(2)	37(1)
C(7)	2706(5)	771(3)	5953(2)	47(2)
C(8)	4881(5)	1730(3)	8878(2)	40(1)
C(9)	8691(5)	1607(3)	7381(3)	48(2)
C(10)	6849(6)	1583(4)	9372(2)	55(2)
C(11)	3652(6)	837(3)	9082(3)	59(2)
C(12)	4098(7)	2773(3)	9125(3)	60(2)
N(2)	5593(4)	- 188(3)	6464(2)	48(1)
N(5)	4396(4)	3420(3)	7234(2)	43(1)
N(6)	7870(5)	3234(3)	6575(2)	51(1)
O(1)	5770(4)	1902(2)	5537(2)	62(1)
O(21)	4982(5)	- 964(2)	6734(2)	79(1)
O(22)	6943(5)	- 186(3)	6131(2)	80(1)
O(51)	4262(4)	4245(2)	7589(2)	63(1)
O(52)	3393(4)	3142(2)	6597(2)	62(1)
O(61)	9198(4)	3071(3)	6248(2)	74(1)
O(62)	7154(5)	4083(3)	6600(2)	85(2)
H(3)	3790(40)	390(20)	7590(20)	15(8)
H(5)	6670(40)	2990(20)	8050(20)	14(8)

TABLE 5. Fractional coordinates for non-constrained atoms in 4-t-butyl-2,6-dimethyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (73), $C_{12}H_{17}N_3O_7$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	2708(3)	2987(3)	6875(1)	33(1)
C(2)	3619(3)	1643(2)	7060(1)	30(1)
C(3)	3089(3)	382(2)	6651(1)	29(1)
C(4)	2121(2)	364(2)	6079(1)	26(1)
C(5)	1524(2)	1745(2)	5786(1)	24(1)
C(6)	1196(2)	2732(2)	6422(1)	27(1)
C(7)	3590(4)	1436(3)	7899(1)	46(1)
C(8)	1506(3)	- 964(3)	5717(1)	37(1)
C(9)	- 103(3)	2175(3)	6920(1)	39(1)
C(10)	2379(5)	-2234(3)	6001(2)	59(1)
C(11)	1682(4)	- 905(3)	4878(2)	54(1)
C(12)	- 250(4)	-1109(4)	5907(2)	60(1)
N(2)	5371(2)	1882(3)	6863(1)	39(1)
N(5)	2803(2)	2347(2)	5289(1)	32(1)
N(6)	644(2)	4146(2)	6130(1)	40(1)
O(1)	3040(2)	4092(2)	7122(1)	57(1)
O(21)	5993(2)	1043(2)	6462(1)	53(1)
O(22)	6032(3)	2859(3)	7135(2)	74(1)
O(51)	3877(2)	2955(2)	5588(1)	46(1)
O(52)	2689(2)	2153(2)	4630(1)	49(1)
O(61)	869(3)	4411(2)	5487(1)	54(1)
O(62)	11(3)	4917(2)	6560(1)	67(1)
H(3)	3460(30)	- 450(30)	6850(10)	40(7)
H(5)	710(20)	1660(20)	5480(10)	10(5)

TABLE 6. Fractional coordinates for non-constrained atoms in 4-t-butyl-*c*-6-hydroxy-2,6-dimethyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (74), $C_{12}H_{18}N_2O_6$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	7765(6)	2265(3)	4307(3)	38(2)
C(2)	7801(6)	3352(3)	4653(3)	41(2)
C(3)	7360(6)	3368(3)	5489(3)	44(2)
C(4)	6883(6)	2563(3)	5914(2)	40(2)
C(5)	6880(6)	1498(3)	5558(3)	38(2)
C(6)	6414(6)	1485(3)	4672(2)	35(1)
C(7)	6395(7)	4065(4)	4140(3)	54(2)
C(8)	6301(7)	2651(4)	6753(3)	50(2)
C(9)	4178(6)	1740(4)	4464(3)	47(2)
C(10)	6540(10)	3744(4)	7072(3)	93(3)
C(11)	7610(10)	1954(5)	7300(3)	86(3)
C(12)	4106(8)	2331(7)	6765(3)	108(3)
N(2)	9949(6)	3763(3)	4609(2)	57(2)
N(5)	8962(5)	1017(3)	5724(2)	47(1)
O(1)	8679(5)	2036(2)	3761(2)	64(1)
O(21)	11091(5)	3761(3)	5202(3)	80(2)
O(22)	10406(6)	4058(3)	3982(3)	92(2)
O(51)	10342(5)	1458(3)	5448(2)	64(1)
O(52)	9145(5)	226(3)	6106(2)	66(1)
O(6)	6755(4)	484(2)	4379(2)	49(1)
H(3)	7370(60)	4000(30)	5670(20)	60(10)
H(5)	6050(50)	1020(30)	5820(20)	23(9)
HO(6)	7800(60)	480(30)	4170(30)	80(14)

TABLE 7. Fractional coordinates for non-constrained atoms in 2-t-butyl-4,6-dimethyl-*r*-4,*c*-5,*t*-6-trinitrocyclohex-2-enone (80), $C_{12}H_{17}N_3O_7$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	7694(3)	3440(4)	160(10)	32(1)
C(2)	7197(3)	4270(4)	- 450(10)	32(1)
C(3)	7495(3)	4993(4)	-1570(11)	31(1)
C(4)	8321(3)	5140(4)	-2211(9)	27(1)
C(5)	8813(3)	4256(4)	-1510(10)	29(1)
C(6)	8406(3)	3293(3)	-1300(10)	27(1)
C(7)	6361(3)	4234(5)	270(10)	41(2)
C(8)	8605(3)	6100(4)	-1290(10)	38(2)
C(9)	8132(3)	2785(4)	-3370(10)	41(2)
C(10)	6002(3)	3307(5)	- 680(10)	66(3)
C(11)	5921(3)	5111(5)	- 630(10)	64(3)
C(12)	6304(4)	4247(6)	2770(10)	67(3)
N(4)	8287(2)	5224(3)	-4758(8)	40(2)
N(5)	9546(2)	4186(4)	-2807(8)	40(2)
N(6)	8908(3)	2607(3)	70(10)	41(2)
O(1)	7549(2)	2872(2)	1614(8)	43(1)
O(41)	8485(2)	4543(3)	-5877(8)	59(2)
O(42)	8057(3)	5971(4)	-5518(9)	80(2)
O(51)	9834(2)	4940(3)	-3390(10)	62(2)
O(52)	9813(2)	3390(3)	-3070(10)	62(2)
O(61)	9276(2)	2971(3)	1550(10)	55(2)
O(62)	8881(2)	1756(3)	- 314(9)	66(2)
H(3)	7240(20)	5620(30)	-2130(80)	38(14)
H(5)	8990(20)	4470(30)	30(80)	33

TABLE 8. Fractional coordinates for non-constrained atoms in 2-t-butyl-4,6-dimethyl-*r*-4,*t*-5,*c*-6-trinitrocyclohex-2-enone (81), $C_{12}H_{17}N_3O_7$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	915(3)	- 182(7)	2815(2)	37(2)
C(2)	- 74(3)	549(6)	2214(2)	34(1)
C(3)	- 749(3)	1659(6)	2436(2)	33(2)
C(4)	- 636(3)	2348(6)	3233(2)	32(1)
C(5)	295(3)	1229(6)	3823(2)	30(1)
C(6)	1250(3)	1110(6)	3576(2)	32(1)
C(7)	- 242(3)	1(7)	1382(2)	40(2)
C(8)	- 672(3)	4812(6)	3299(2)	48(2)
C(9)	1754(3)	3219(7)	3465(2)	52(2)
C(10)	-1281(3)	934(8)	853(2)	57(2)
C(11)	- 252(4)	-2448(8)	1260(3)	63(2)
C(12)	649(3)	1070(8)	1184(2)	59(2)
N(4)	-1642(3)	1382(7)	3335(2)	43(2)
N(5)	536(2)	2255(5)	4603(2)	40(1)
N(6)	2060(2)	- 349(6)	4151(2)	47(1)
O(1)	1492(2)	-1548(5)	2728(1)	61(1)
O(41)	-1665(2)	- 543(6)	3454(2)	63(1)
O(42)	-2376(2)	2604(6)	3224(2)	72(2)
O(51)	- 205(2)	2432(5)	4819(1)	52(1)
O(52)	1413(2)	2805(6)	4968(2)	70(1)
O(61)	1736(2)	-1935(5)	4384(2)	67(1)
O(62)	2970(2)	103(6)	4310(2)	74(1)
H(3)	-1390(30)	2120(60)	2060(20)	42(11)
H(5)	100(20)	- 130(40)	3890(20)	19(8)

TABLE 9. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*t*-6-trinitrocyclohex-3-enone (86), $C_{15}H_{23}N_3O_7$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	2678(5)	1469(3)	7143(5)	65(3)
C(2)	2025(4)	978(2)	7240(5)	49(2)
C(3)	1315(5)	946(3)	6193(5)	46(2)
C(4)	1283(4)	1222(2)	5132(5)	40(2)
C(5)	2073(5)	1631(3)	4906(6)	54(2)
C(6)	2463(5)	1883(2)	6089(6)	62(3)
C(7)	1512(5)	900(3)	8590(5)	69(3)
C(8)	524(5)	1163(2)	4120(5)	50(2)
C(9)	3355(6)	2230(3)	5875(8)	108(4)
C(10)	2215(6)	1000(4)	9679(6)	108(4)
C(11)	701(5)	1300(4)	8669(7)	113(4)
C(12)	1092(7)	341(3)	8699(8)	126(5)
C(13)	951(7)	1117(3)	2819(6)	104(4)
C(14)	- 114(6)	687(3)	4368(7)	98(4)
C(15)	- 136(6)	1662(3)	4144(7)	98(4)
N(2)	2708(4)	486(2)	7090(4)	77(2)
N(5)	2941(4)	1361(2)	4256(5)	80(3)
N(6)	1683(5)	2255(2)	6594(5)	98(3)
O(1)	3356(4)	1530(2)	7814(4)	115(3)
O(21)	2421(4)	130(2)	6435(5)	112(3)
O(22)	3461(4)	475(3)	7663(5)	132(3)
O(51)	3348(4)	1011(2)	4839(5)	98(2)
O(52)	3151(4)	1517(3)	3219(5)	143(3)
O(61)	1771(6)	2376(2)	7717(6)	163(4)
O(62)	1089(5)	2426(2)	5939(6)	150(3)
H(3)	820(30)	670(20)	6240(50)	50(20)
H(5)	1880(30)	1880(20)	4350(30	20(10)

TABLE 10. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-6-methyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (87), $C_{15}H_{23}N_3O_7$ (molecule one).

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	8538	3055(4)	1207(3)	33(1)
C(2)	8231(3)	2156(4)	1575(3)	35(1)
C(3)	8480(3)	2362(4)	2465(3)	38(1)
C(4)	8904(3)	3169(4)	2907(3)	36(1)
C(5)	9186(3)	4065(4)	2523(3)	38(1)
C(6)	9349(3)	3634(4)	1822(3)	36(1)
C(7)	7259(3)	1818(4)	1074(3)	46(2)
C(8)	9173(4)	3251(5)	3822(3)	56(3)
C(9)	10155(3)	2936(4)	2171(3)	51(3)
C(10)	7004(4)	964(5)	1520(4)	76(3)
C(11)	7069(4)	1405(5)	225(3)	74(3)
C(12)	6694(3)	2791(4)	981(4)	74(3)
C(13)	8869(6)	4248(6)	4045(4)	133(6)
C(14)	8893(6)	2296(6)	4137(4)	124(5)
C(15)	10144(4)	3270(7)	4261(4)	117(4)
N(2)	8776(3)	1177(4)	1558(3)	49(2)
N(5)	8484(3)	4915(3)	2240(3)	57(2)
N(6)	9540(3)	4524(3)	1354(2)	56(2)
O(1)	8191(2)	3313(3)	511(2)	52(2)
O(21)	8906(3)	480(3)	2051(3)	76(2)
O(22)	9029(3)	1174(3)	1030(3)	75(2)
O(51)	7816(2)	4692(3)	1651(2)	78(2)
O(52)	8642(3)	5743(3)	2606(2)	94(2)
O(61)	9816(2)	4265(3)	877(2)	79(2)
O(62)	9371(3)	5424(3)	1462(2)	88(2)
H(3)	8350(20)	1760(30)	2700(20)	40(10)
H(5)	9680(30)	4410(30)	2930(20)	40(10)

TABLE 11. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-6-methyl-*r*-2,*t*-5,*t*-6-trinitrocyclohex-3-enone (87), $C_{15}H_{23}N_3O_7$(molecule <u>two</u>).

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(16)	6639(3)	6039(4)	8142(3)	39(1)
C(17)	5919(3)	5685(4)	8372(3)	37(1)
C(18)	6018(3)	6225(4)	9143(3)	43(1)
C(19)	6619(3)	6892(4)	9601(3)	37(1)
C(20)	7342(3)	7182(4)	9374(3)	40(1)
C(21)	7489(3)	6309(4)	8871(3)	40(1)
C(22)	4982(3)	5754(4)	7667(3)	47(3)
C(23)	6594(3)	7406(4)	10351(3)	45(2)
C(24)	7925(3)	5381(4)	9430(3)	59(3)
C(25)	4330(4)	5339(5)	7965(4)	78(3)
C(26)	4860(3)	5109(5)	6918(3)	63(3)
C(27)	4793(4)	6909(4)	7430(4)	89(4)
C(28)	6173(4)	6676(5)	10743(3)	70(3)
C(29)	7503(3)	7703(5)	11006(3)	75(3)
C(30)	6041(4)	8419(4)	10080(3)	65(3)
N(2')	6109(3)	4490(4)	8581(3)	55(2)
N(5')	7119(3)	8234(4)	8919(4)	56(3)
N(6')	8113(3)	6646(4)	8534(3)	57(3)
O(1')	6540(2)	6127(3)	7451(2)	60(2)
O(21')	6448(3)	4009(3)	8217(2)	72(2)
O(22')	5907(3)	4100(3)	9076(2)	84(2)
O(51')	6600(2)	8207(3)	8210(2)	75(2)
O(52')	7460(3)	9023(3)	9309(3)	82(2)
O(61')	8432(2)	7518(3)	8710(2)	76(2)
O(62')	8288(3)	5991(4)	8141(3)	84(3)
H(18)	5570(30)	6000(30)	9260(20)	40(10)
H(20)	7860(30)	7340(30)	9840(20)	30(10)

TABLE 12. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-6-methyl-*r*-2,*c*-5,*c*-6-trinitrocyclohex-3-enone (88), $C_{15}H_{23}N_3O_7$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	4482(3)	1229(4)	8135(2)	44(2)
C(2)	3569(3)	1767(4)	7925(2)	41(2)
C(3)	2803(3)	1568(4)	8413(2)	41(2)
C(4)	2878(3)	1215(3)	9043(2)	37(2)
C(5)	3842(3)	1012(4)	9318(2)	43(2)
C(6)	4441(3)	506(4)	8768(2)	42(2)
C(7)	3265(3)	1490(4)	7175(2)	50(2)
C(8)	2050(3)	976(4)	9505(2)	46(2)
C(9)	4098(3)	- 632(3)	8606(2)	52(2)
C(10)	2993(4)	312(5)	7155(3)	85(3)
C(11)	4032(4)	1675(5)	6654(3)	85(3)
C(12)	2441(4)	2178(5)	6957(3)	79(2)
C(13)	1144(3)	1151(5)	9145(3)	72(2)
C(14)	2084(3)	- 192(4)	9746(3)	62(2)
C(15)	2101(4)	1707(5)	10126(3)	79(3)
N(2)	3757(3)	3007(3)	7929(2)	54(1)
N(5)	4248(3)	2075(4)	9559(2)	59(2)
N(6)	5436(3)	366(3)	9013(2)	56(2)
O(1)	5182(2)	1306(3)	7822(2)	68(1)
O(21)	3140(2)	3562(3)	8153(2)	74(1)
O(22)	4469(3)	3341(3)	7701(2)	80(2)
O(51)	4523(3)	2692(3)	9134(2)	70(1)
O(52)	4272(3)	2237(4)	10159(2)	104(2)
O(61)	5679(2)	865(3)	9507(2)	89(2)
O(62)	5928(2)	- 254(3)	8722(2)	96(2)
H(3)	2190(15)	1700(30)	8280(20)	40(10)
H(5)	3810(20)	580(20)	9710(10)	30(10)

TABLE 13. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*c*-6-dinitrocyclohex-3-enone (89), $C_{15}H_{24}N_2O_6$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	8276(4)	3780(2)	3261(4)	43(2)
C(2)	8201(4)	3916(2)	4807(4)	44(2)
C(3)	6513(4)	3954(2)	4527(5)	44(2)
C(4)	5198(4)	3913(2)	3180(4)	44(2)
C(5)	5325(5)	3822(2)	1670(4)	49(2)
C(6)	6888(4)	4023(2)	1732(4)	43(2)
C(7)	9196(5)	3468(2)	6180(4)	53(2)
C(8)	3560(4)	3959(2)	3083(5)	56(2)
C(9)	7065(6)	3855(2)	266(5)	65(2)
C(10)	10958(5)	3487(3)	6601(6)	73(2)
C(11)	9034(6)	3658(3)	7659(5)	85(3)
C(12)	8619(6)	2800(2)	5727(6)	74(3)
C(13)	3633(6)	4027(3)	4721(6)	98(3)
C(14)	2699(6)	4530(3)	2107(7)	93(3)
C(15)	2609(5)	3372(3)	2305(7)	94(3)
N(5)	5148(4)	3135(2)	1218(4)	64(2)
N(6)	6957(5)	4738(2)	1819(4)	57(2)
O(1)	9331(3)	3519(2)	3154(4)	67(1)
O(2)	8770(3)	4554(1)	5168(3)	55(1)
O(51)	5974(4)	2765(1)	2179(4)	75(2)
O(52)	4204(4)	3002(2)	- 117(4)	114(2)
O(61)	5836(4)	5030(1)	1753(4)	74(2)
O(62)	8174(5)	4975(2)	1918(4)	81(2)
H(3)	6440(40)	4060(20)	5470(30)	60(12)
H(5)	4490(30)	4040(10)	850(30)	30(10)
HO(2)	9880(24)	4580(32)	5660(70)	160(30)

TABLE 14. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-*r*-2-hydroxy-6-methyl-*t*-5,*t*-6-dinitrocyclohex-3-enone (90), $C_{15}H_{24}N_2O_6$.

Atom	$10^4X/a$	$10^4Y/b$	$10^4Z/c$	10^3U
C(1)	0(3)	7755(5)	4032(3)	40(2)
C(2)	- 961(3)	7728(5)	3508(2)	35(1)
C(3)	- 744(3)	7563(5)	2632(2)	37(1)
C(4)	109(3)	7394(5)	2294(2)	34(1)
C(5)	1043(3)	7346(5)	2825(2)	37(1)
C(6)	915(3)	8407(5)	3593(2)	36(1)
C(7)	-1760(3)	6359(6)	3757(2)	42(1)
C(8)	218(3)	7388(7)	1379(2)	55(2)
C(9)	843(3)	10399(6)	3400(3)	51(2)
C(10)	-2682(3)	6624(7)	3201(3)	62(2)
C(11)	-1393(4)	4449(6)	3675(3)	60(2)
C(12)	-2071(4)	6631(7)	4626(3)	69(2)
C(13)	- 762(4)	7202(8)	921(3)	79(2)
C(14)	620(5)	9265(9)	1153(3)	108(3)
C(15)	946(5)	6090(11)	1096(3)	142(4)
N(5)	1300(3)	5420(5)	3019(2)	46(1)
N(6)	1826(3)	8201(6)	4169(2)	49(2)
O(1)	38(2)	7491(5)	4740(2)	63(1)
O(2)	-1330(2)	9525(4)	3585(2)	44(1)
O(51)	1946(3)	4708(5)	2653(2)	72(1)
O(52)	823(2)	4706(4)	3527(2)	64(1)
O(61)	2463(2)	7175(5)	3991(2)	71(1)
O(62)	1862(2)	9119(5)	4768(2)	74(1)
H(3)	-1300(20)	7530(50)	2290(20)	50(10)
H(5)	1590(20)	7800(50)	2540(20)	30(10)
HO(2)	-1500(30)	9810(60)	4120(25)	90(10)

TABLE 15. Fractional coordinates for non-constrained atoms in 2,4-di-t-butyl-*c*-6-hydroxy-6-methyl-*r*-2,*c*-5-dinitrocyclohex-3-enone (91), $C_{15}H_{24}N_2O_6$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	4504(2)	1019(2)	6995(2)	38(1)
C(2)	3456(2)	1220(2)	7288(2)	33(1)
C(3)	2692(2)	1054(2)	6698(2)	33(1)
C(4)	2813(2)	607(2)	6056(2)	32(1)
C(5)	3804(3)	177(3)	5877(2)	38(1)
C(6)	4645(3)	800(3)	6170(2)	41(1)
C(7)	3349(2)	2258(3)	7671(2)	40(1)
C(8)	2015(2)	517(3)	5467(2)	37(1)
C(9)	4706(3)	1752(3)	5722(2)	56(2)
C(10)	2313(3)	2403(3)	7994(2)	55(2)
C(11)	4085(3)	2427(3)	8299(2)	69(2)
C(12)	3511(3)	3046(3)	7072(2)	65(2)
C(13)	1011(3)	814(3)	5766(2)	61(2)
C(14)	1949(3)	- 539(3)	5168(2)	60(2)
C(15)	2279(3)	1211(3)	4829(2)	62(2)
N(2)	3249(2)	454(2)	7909(2)	40(1)
N(5)	3886(2)	- 845(2)	6222(2)	47(1)
O(1)	5216(2)	1049(2)	7380(1)	55(1)
O(21)	2412(2)	140(2)	7952(1)	55(1)
O(22)	3901(2)	210(2)	8321(1)	67(1)
O(51)	3942(2)	- 878(2)	6895(1)	57(1)
O(52)	3898(2)	-1564(2)	5826(2)	72(1)
O(6)	5524(2)	251(2)	6072(1)	54(1)
H(3)	2090(20)	1320(20)	6820(10)	31(8)
H(5)	3910(20)	60(20)	5390(10)	12(8)
HO(6)	5920(20)	360(30)	6470(15)	65

TABLE 16. Fractional coordinates for non-constrained atoms in 2,6-di-t-butyl-4-methyl-*r*-4,*c*-5,*c*-6-trinitrocyclohex-2-enone (95), $C_{15}H_{23}N_3O_7$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	- 207(9)	632(3)	7064(4)	36(2)
C(2)	-1722(7)	218(2)	7537(4)	34(2)
C(3)	-2223(9)	410(3)	8394(4)	42(2)
C(4)	-1416(8)	1016(2)	8926(3)	38(2)
C(5)	-1266(7)	1563(3)	8164(4)	36(2)
C(6)	- 146(7)	1397(3)	7255(3)	34(2)
C(7)	-2448(9)	- 449(3)	7096(4)	49(2)
C(8)	-3150(10)	- 376(3)	6004(4)	82(2)
C(9)	-4309(8)	- 721(3)	7594(4)	74(3)
C(10)	- 593(9)	- 931(3)	7231(5)	80(3)
C(11)	-2827(8)	1219(3)	9702(4)	59(3)
C(12)	-1109(8)	1769(2)	6317(3)	43(2)
C(13)	-3249(8)	1427(3)	6003(4)	62(2)
C(14)	-1590(10)	2493(3)	6509(4)	70(3)
C(15)	228(9)	1707(3)	5466(4)	73(3)
N(4)	749(7)	842(3)	9488(3)	47(2)
N(5)	- 560(10)	2218(3)	8650(4)	58(3)
N(6)	2217(6)	1554(2)	7455(3)	50(2)
O(1)	968(6)	409(2)	6511(3)	58(2)
O(41)	1613(7)	343(2)	9298(3)	82(2)
O(42)	1434(6)	1231(2)	10072(3)	115(2)
O(51)	-1969(8)	2576(2)	8865(3)	94(2)
O(52)	1255(8)	2323(3)	8838(4)	117(3)
O(61)	2882(6)	2074(2)	7175(3)	82(2)
O(62)	3298(5)	1153(2)	7922(3)	77(2)
H(3)	-3060(50)	160(20)	8770(30)	9(13)

TABLE 17. Fractional coordinates for non-constrained atoms in 2,6-di-t-butyl-*c*-6-hydroxy-4-methyl-*r*-4,*c*-5-dinitrocyclohex-2-enone (96), $C_{15}H_{24}N_2O_6$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	290(6)	1713(5)	6260(10)	39(3)
C(2)	- 552(6)	1522(5)	5510(10)	43(3)
C(3)	- 873(5)	2031(5)	4070(10)	40(3)
C(4)	- 392(5)	2752(4)	3300(10)	36(3)
C(5)	536(5)	2515(5)	2960(10)	41(3)
C(6)	985(5)	2025(5)	4750(10)	43(3)
C(7)	-1092(6)	848(5)	6470(10)	50(3)
C(8)	- 571(7)	103(5)	6800(20)	73(4)
C(9)	-1843(7)	651(7)	5090(20)	80(5)
C(10)	-1438(7)	1131(7)	8580(10)	73(4)
C(11)	- 779(6)	3111(6)	1390(10)	58(4)
C(12)	1506(6)	1293(5)	3900(10)	54(4)
C(13)	977(7)	715(5)	2690(20)	65(4)
C(14)	2246(6)	1608(7)	2470(20)	71(4)
C(15)	1925(7)	836(6)	5720(20)	68(4)
N(4)	-467(5)	3396(4)	5100(10)	55(3)
N(5)	1050(5)	3237(5)	2310(10)	58(3)
O(1)	489(4)	1629(4)	8090(10)	61(3)
O(41)	- 115(4)	3226(3)	6730(10)	64(2)
O(42)	- 889(5)	3981(4)	4780(10)	82(3)
O(51)	1460(5)	3191(4)	690(10)	81(3)
O(52)	975(5)	3844(4)	3330(10)	81(3)
O(6)	1541(4)	2530(4)	5920(10)	68(3)
H(3)	-1500(40)	2110(30)	3800(900)	30(20)
HO(6)	1820(50)	2760(50)	5900(100)	80(30)

TABLE 18. Fractional coordinates for non-constrained atoms in 4-t-butyl-*r*-2-(4'-t-butyl-2',6'-dimethylphenoxy)-*t*-6-hydroxy-2,6-dimethyl-*t*-5-nitrocyclohex-3-enone (109), $C_{24}H_{35}NO_5$.

Atom	10^4X/a	10^4Y/b	10^4Z/c	10^3U
C(1)	8278(3)	13002(4)	1111(2)	49(1)
C(2)	8556(3)	11615(4)	1432(2)	43(1)
C(3)	9764(3)	11334(5)	1472(2)	45(1)
C(4)	10535(3)	12131(4)	1236(2)	41(1)
C(5)	10218(3)	13503(4)	934(2)	41(1)
C(6)	9050(3)	13544(4)	611(2)	46(1)
C(7)	8094(4)	11518(4)	2112(2)	62(2)
C(8)	11735(3)	11715(4)	1237(2)	52(2)
C(9)	8990(4)	12655(5)	- 17(2)	62(2)
C(10)	11959(4)	10359(5)	1618(3)	88(3)
C(11)	12029(4)	11522(6)	519(3)	93(3)
C(12)	12463(4)	12834(5)	1568(3)	79(2)
C(13)	7278(3)	9645(4)	1134(2)	42(1)
C(14)	6178(4)	9950(5)	1000(2)	55(1)
C(15)	5408(4)	8927(5)	1130(2)	57(1)
C(16)	5705(3)	7645(4)	1374(2)	47(1)
C(17)	6815(3)	7384(4)	1486(2)	52(1)
C(18)	7607(3)	8371(4)	1375(2)	46(1)
C(19)	5797(4)	11322(5)	714(3)	90(3)
C(20)	4859(4)	6513(5)	1479(3)	59(2)
C(21)	8803(3)	7982(5)	1505(3)	66(2)
C(22)	4895(5)	5480(6)	921(3)	127(3)
C(23)	3700(4)	7065(6)	1465(3)	107(3)
C(24)	5112(6)	5752(8)	2119(3)	161(4)
N(5)	10278(3)	14613(4)	1471(2)	52(2)
O(1)	7482(2)	13675(3)	1227(2)	73(1)
O(2)	8067(2)	10603(3)	956(1)	49(1)
O(51)	9707(2)	14450(3)	1940(1)	68(1)
O(52)	10875(2)	15599(3)	1408(1)	71(1)
O(6)	8765(2)	14925(3)	441(1)	62(1)
HO(6)	8190(40)	15050(60)	690(30)	153(20)

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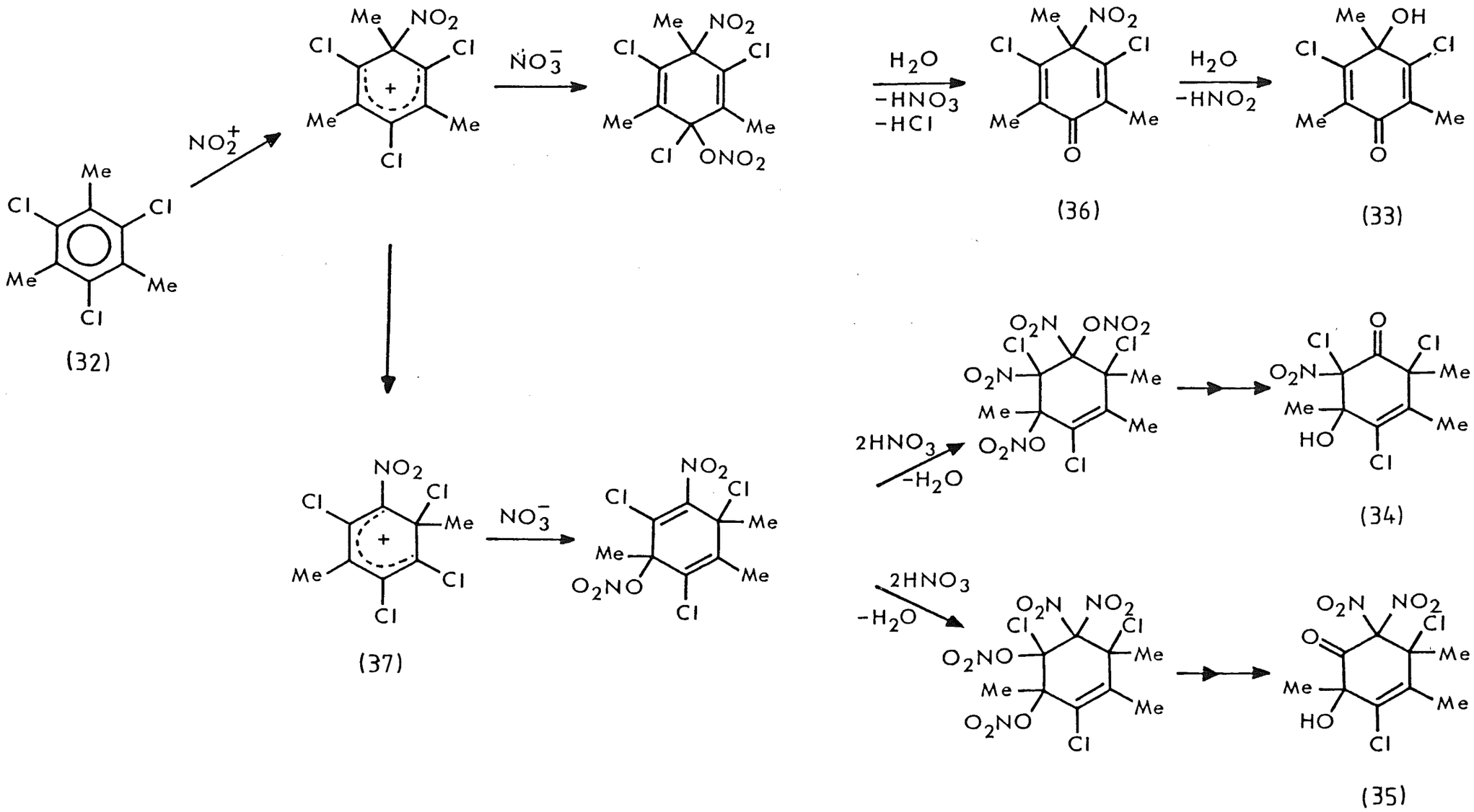
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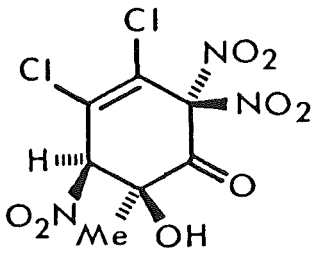
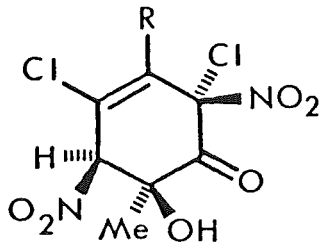
(34)
$2HNO_3$
$-H_2O$
O_2N
NO_2
Cl
Cl
O_2NO
Me
Me
Me
O_2NO
Cl
O
O_2N
NO_2
Cl
Me
Me
Me
HO
Cl
(35)

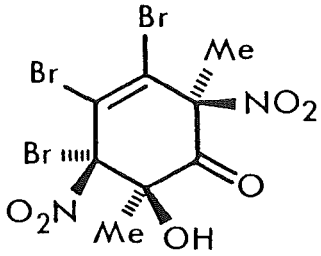
SCHEME 7.



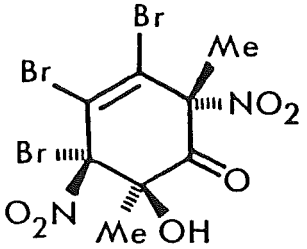
(38)



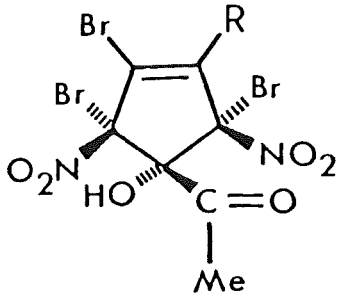
(39) R = H
(40) R = Cl



(29)

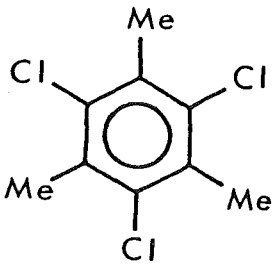


(30)

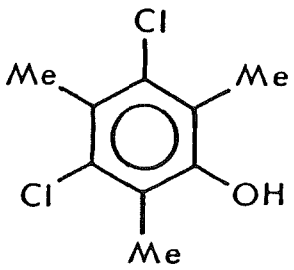


(9) R=Me
(11) R=Br

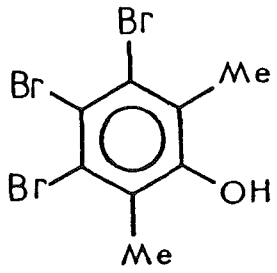
BLOCK C.



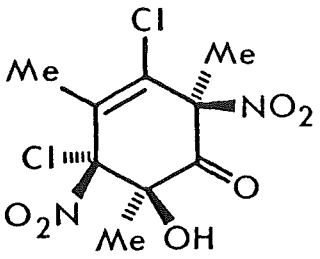
(32)



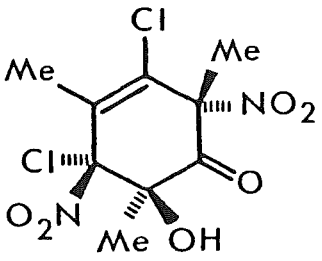
(41)



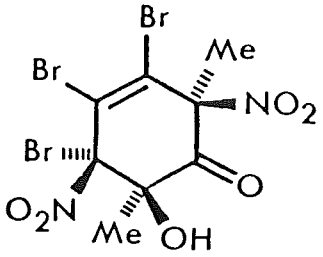
(28)



(42)



(43)



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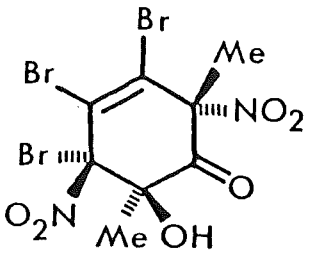
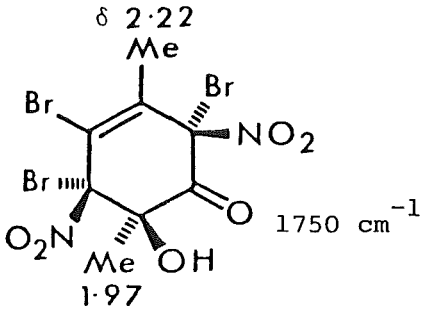


(30)

BLOCK D.



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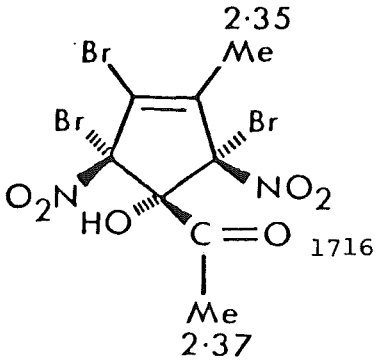
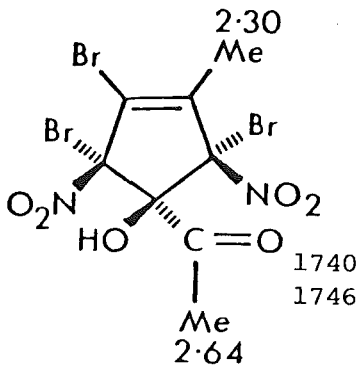
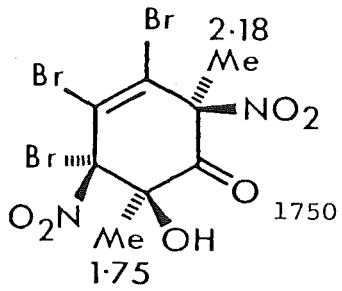


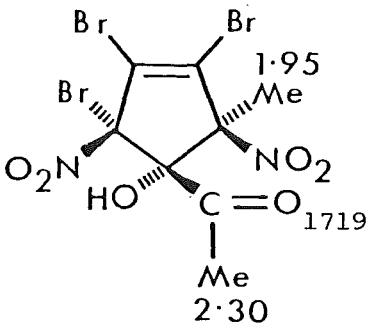
(9)



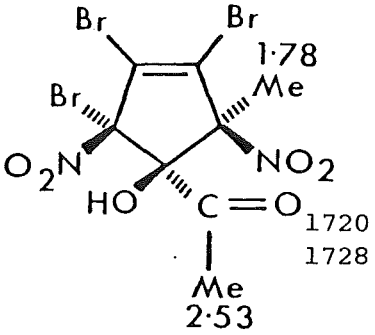
(45)



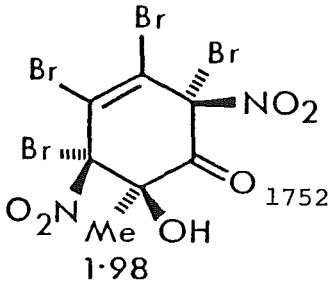
(29)



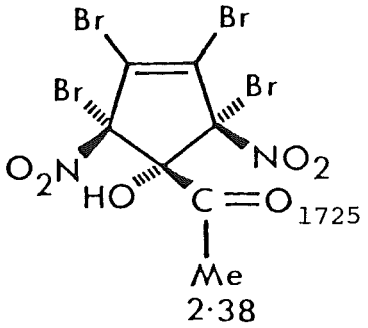
(46)



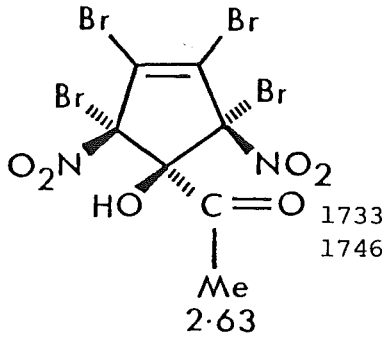
(47)



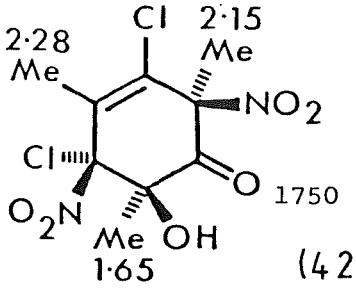
(10)



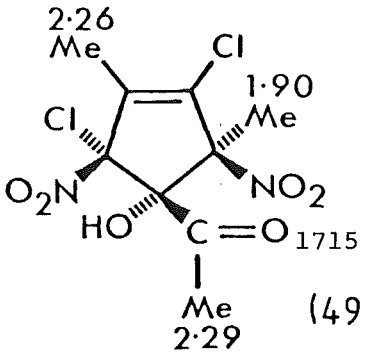
(11)



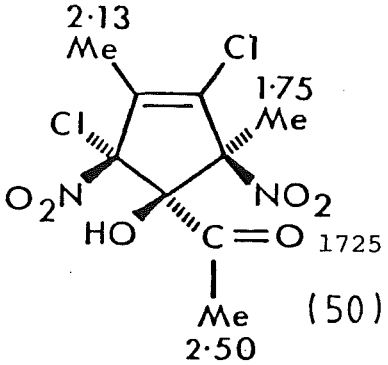
(48)



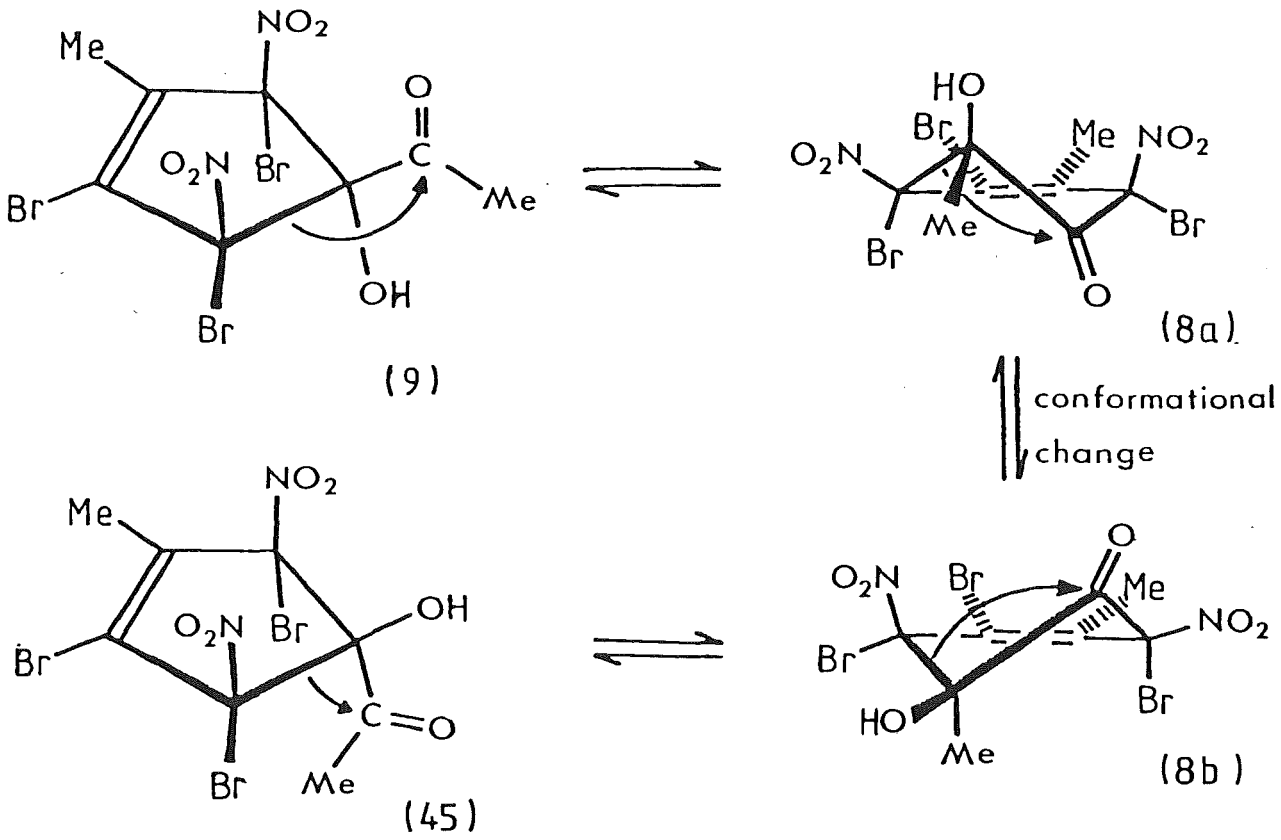
(42)



(49)

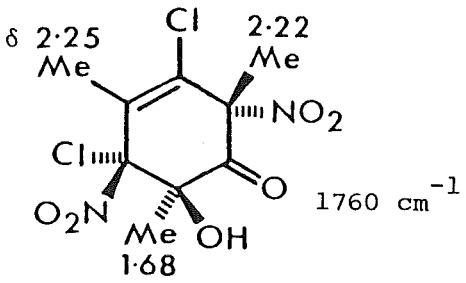


(50)

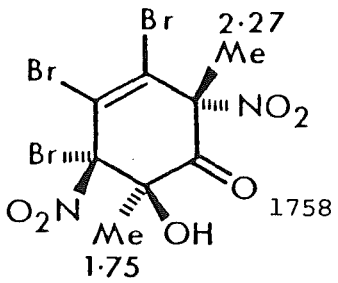

Me
NO2
O
C
Me
O2N
Br
Br
Br
OH
(9)
HO
Br
Me
NO2
O2N
Br
Me
Br
O
(8a)
conformational
change
Me
NO2
OH
O2N
Br
Br
C=O
Br
Me
(45)
O
O2N
Br
Me
NO2
Br
HO
Br
Me
(8b)

SCHEME 8.

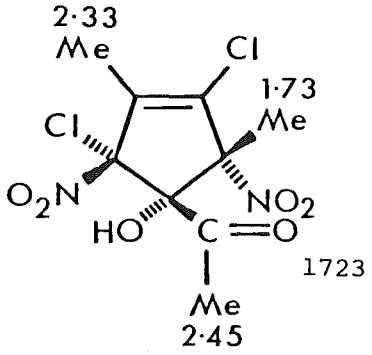
BLOCK E.



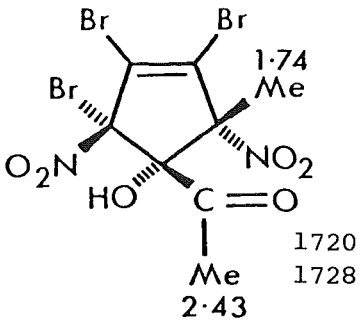
(43)



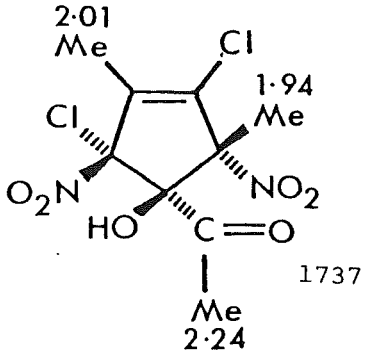
(30)



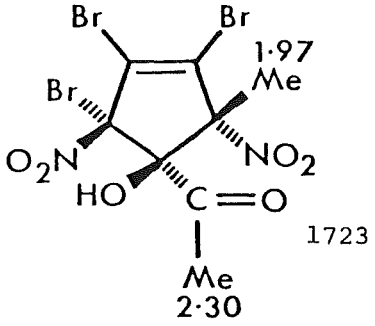
(51)



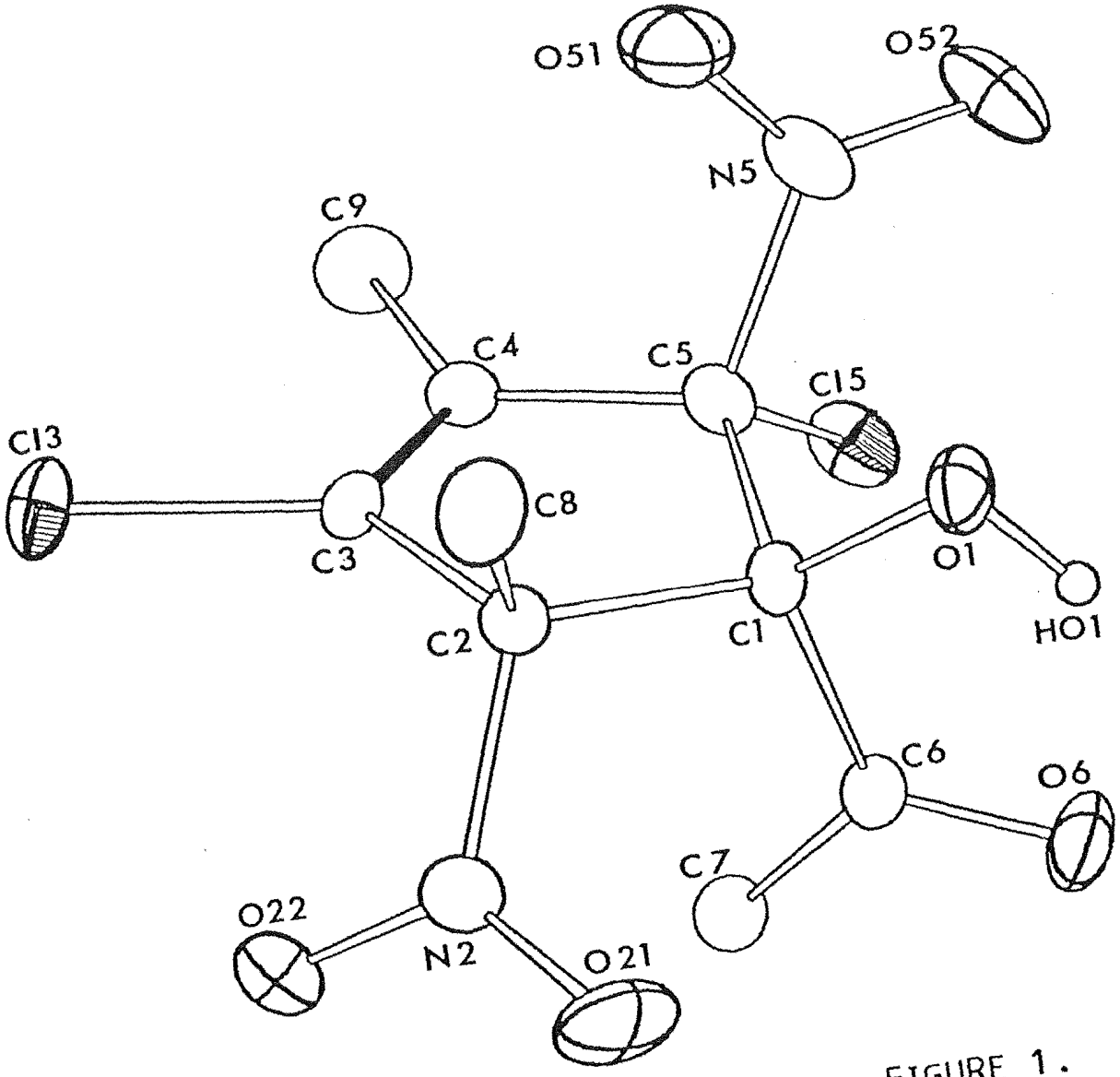
(52)



(44)

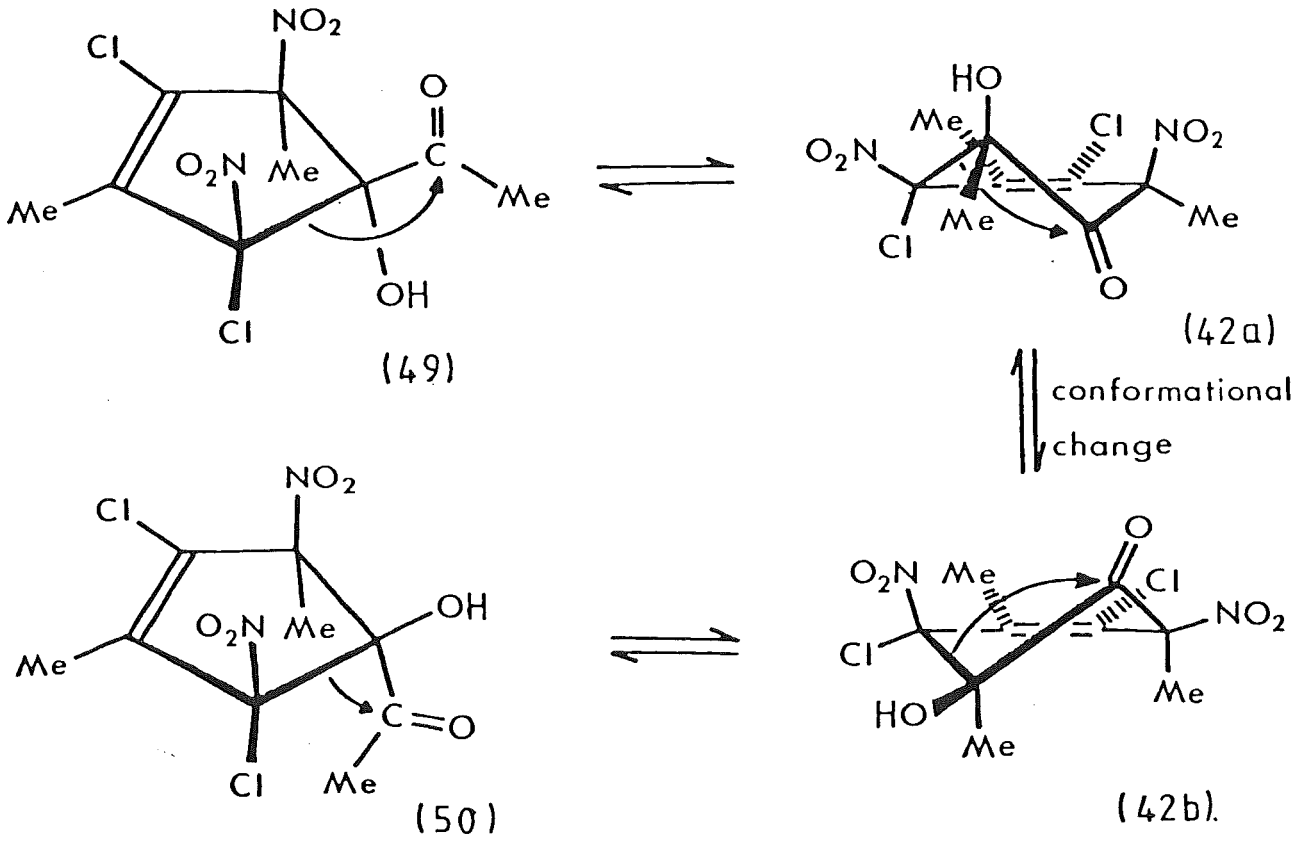


(53)

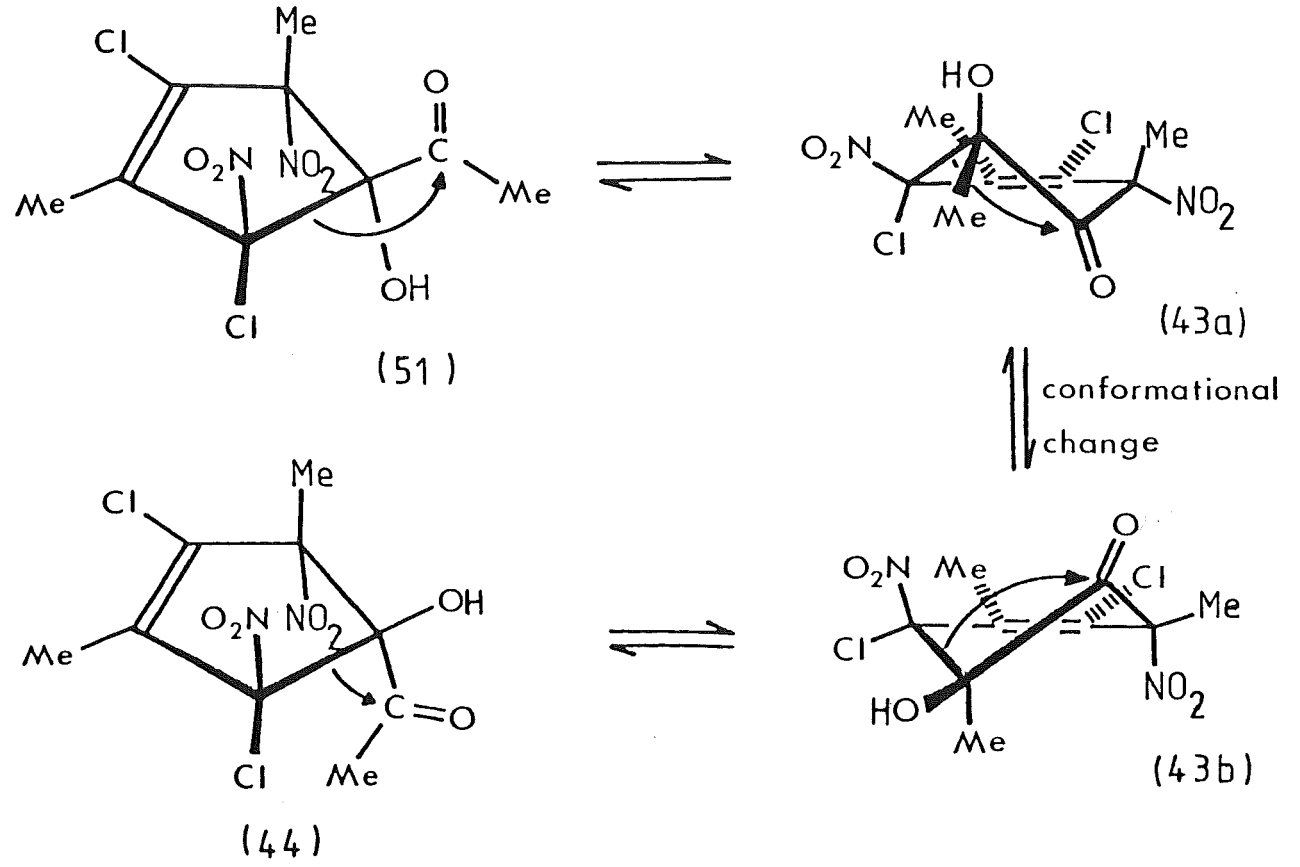


compound (44)

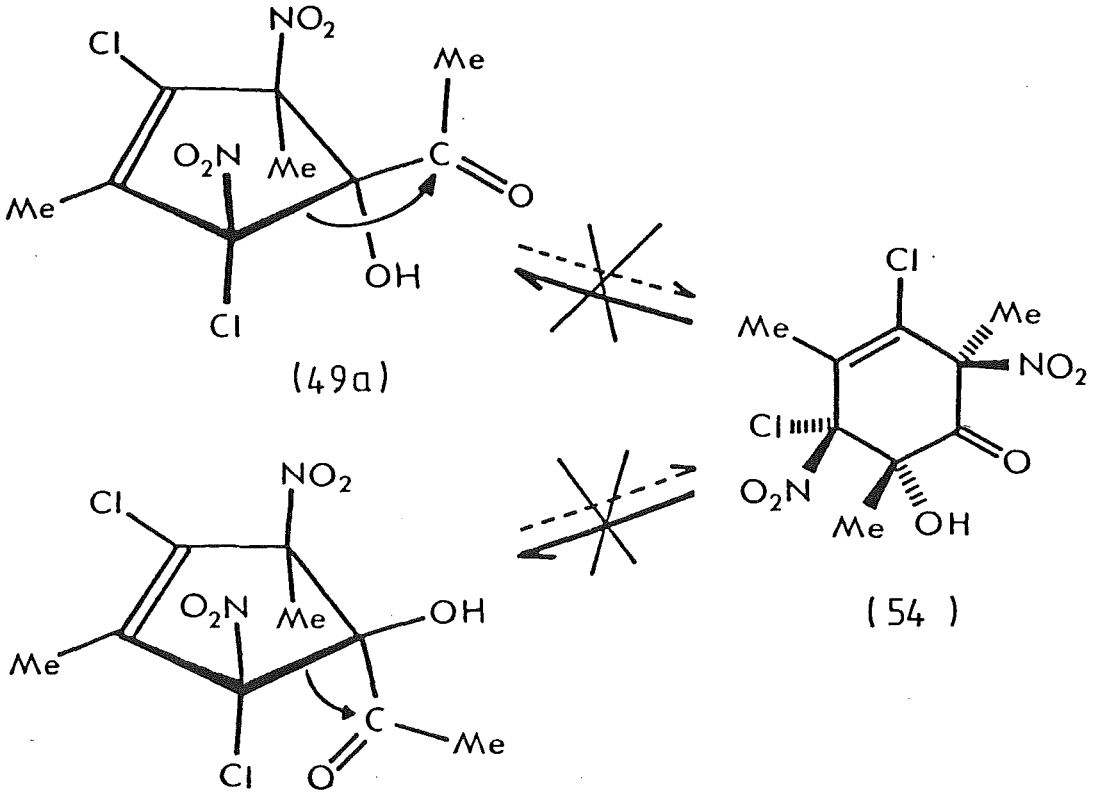
FIGURE 1.



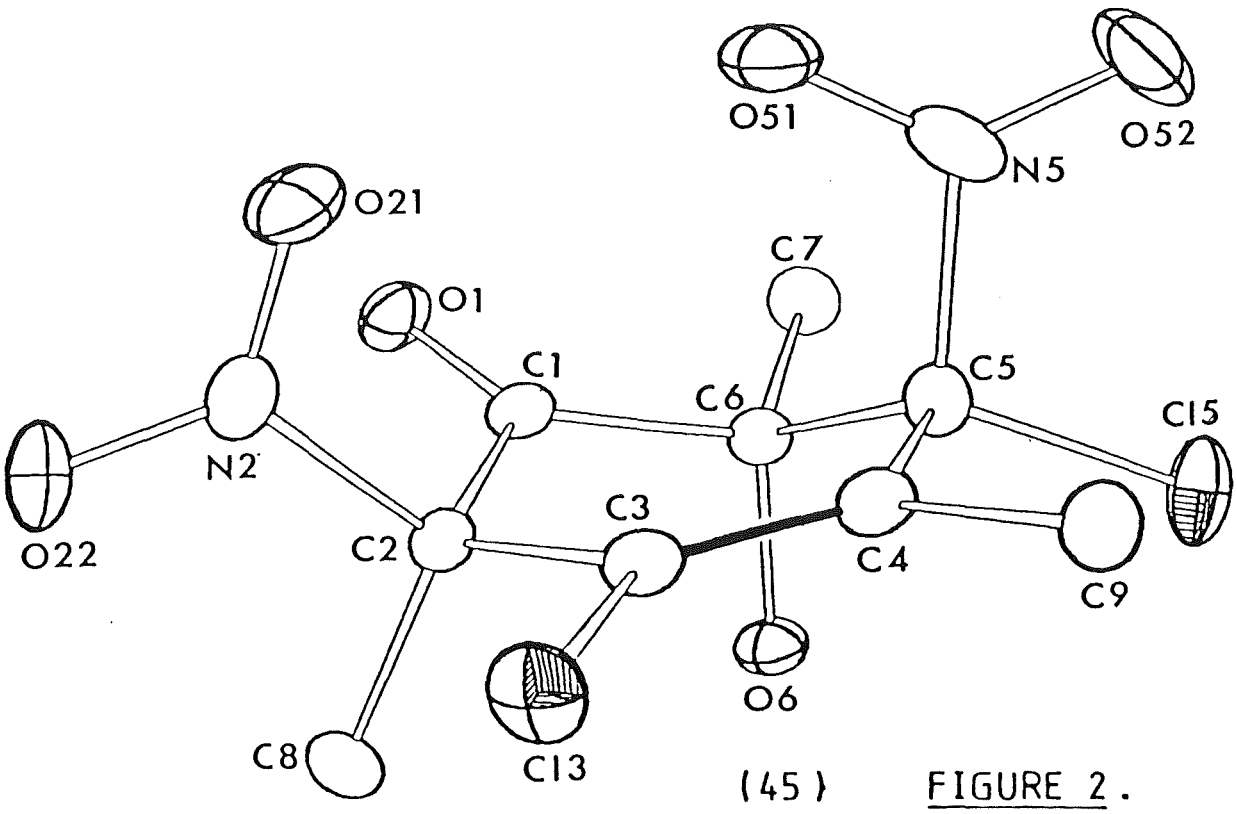
SCHEME 9.



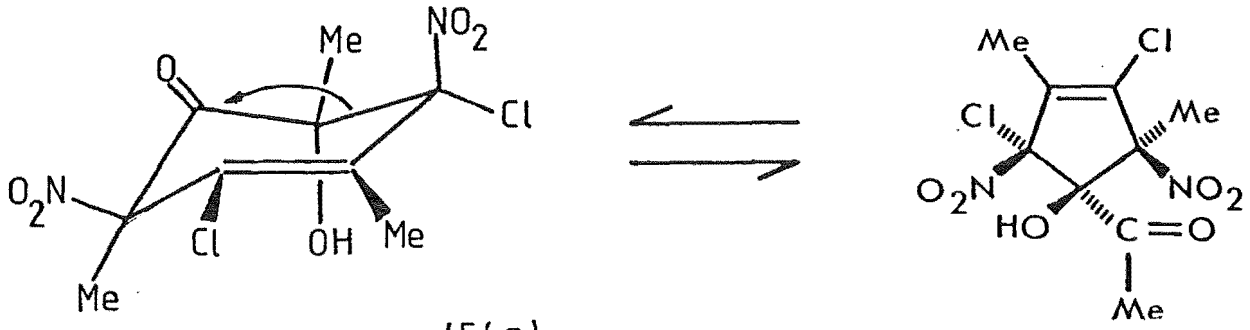
SCHEME 10.



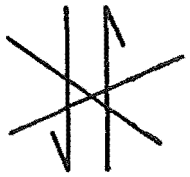
SCHEME 11.



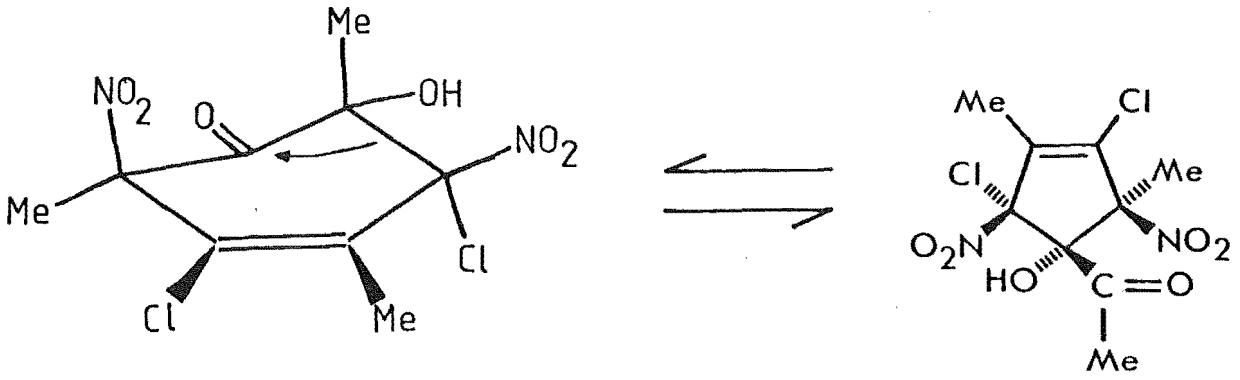
(45) FIGURE 2.



(54a) (50)



conformational change



(54b) (49)

SCHEME 12.

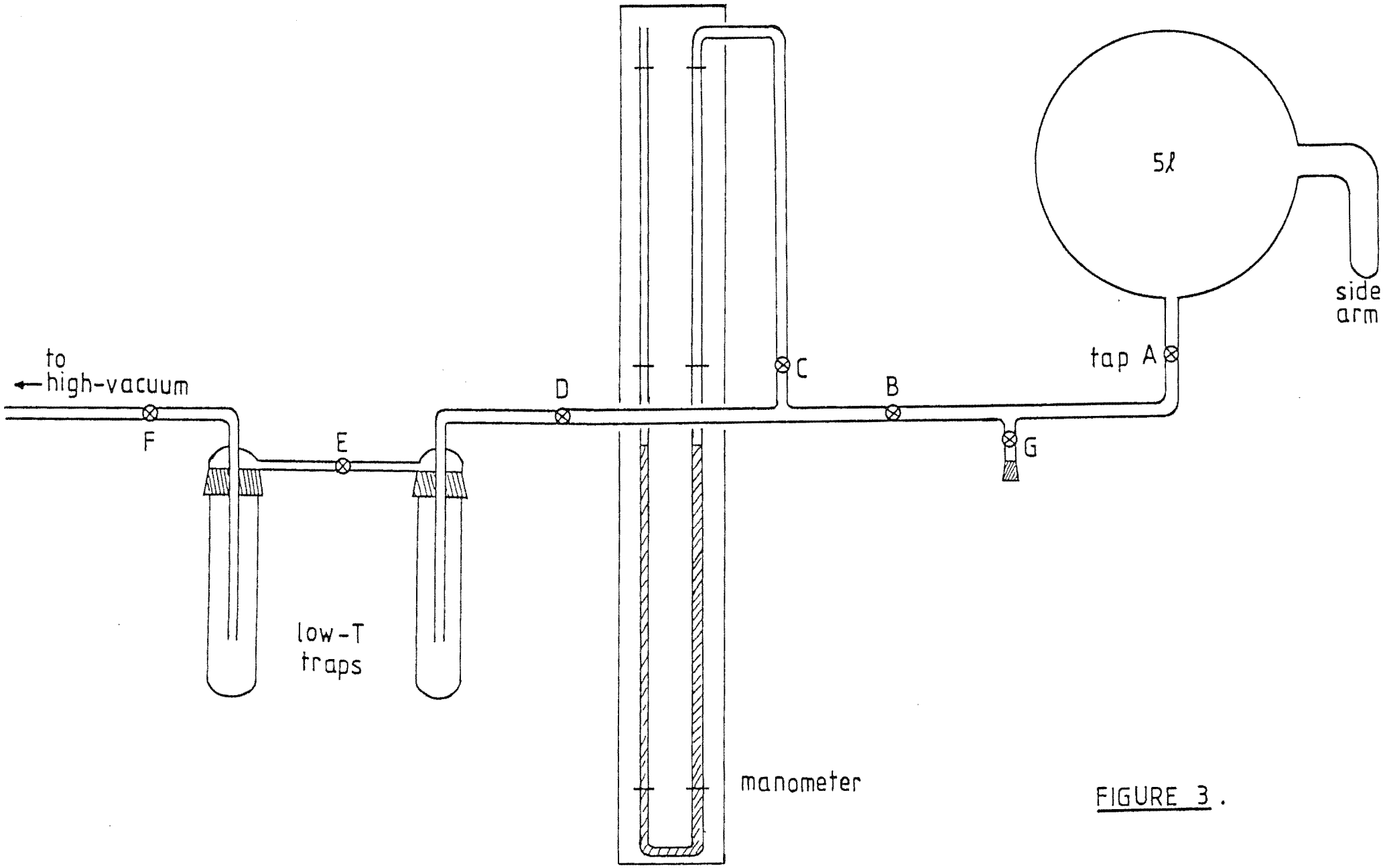


FIGURE 3.

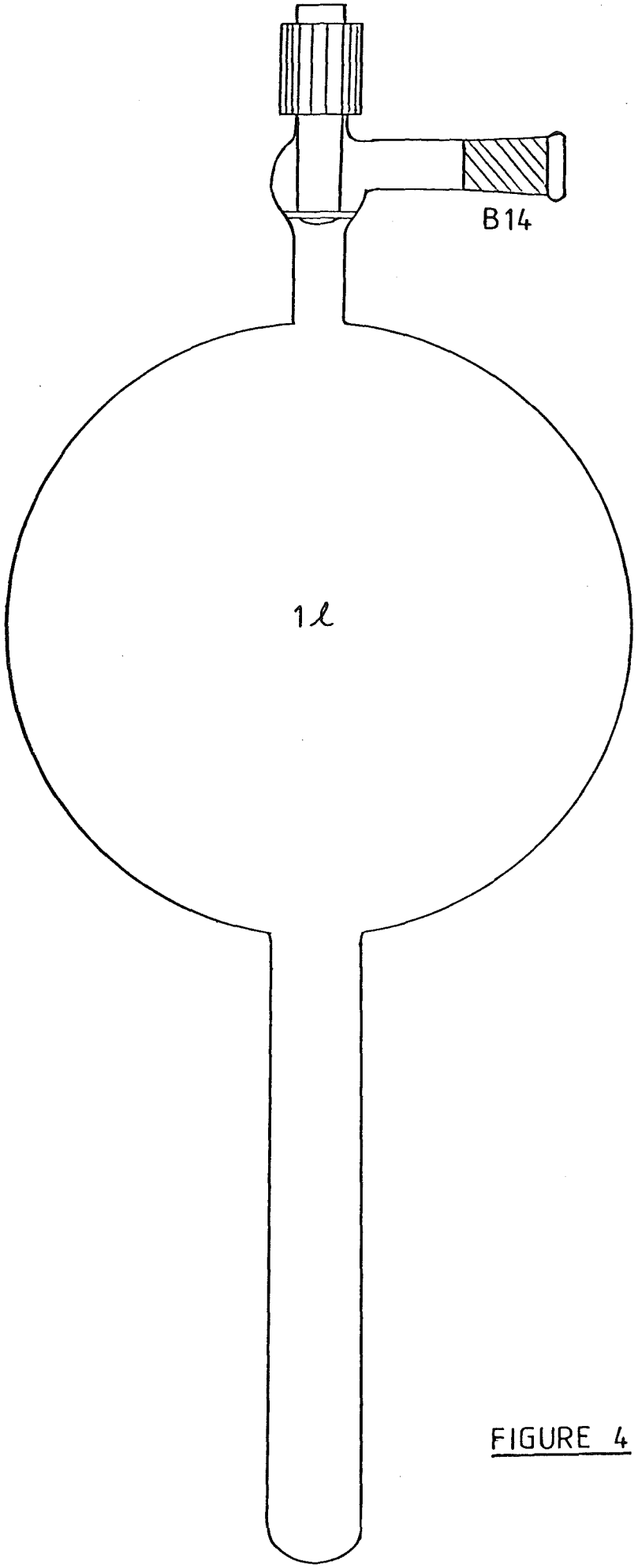
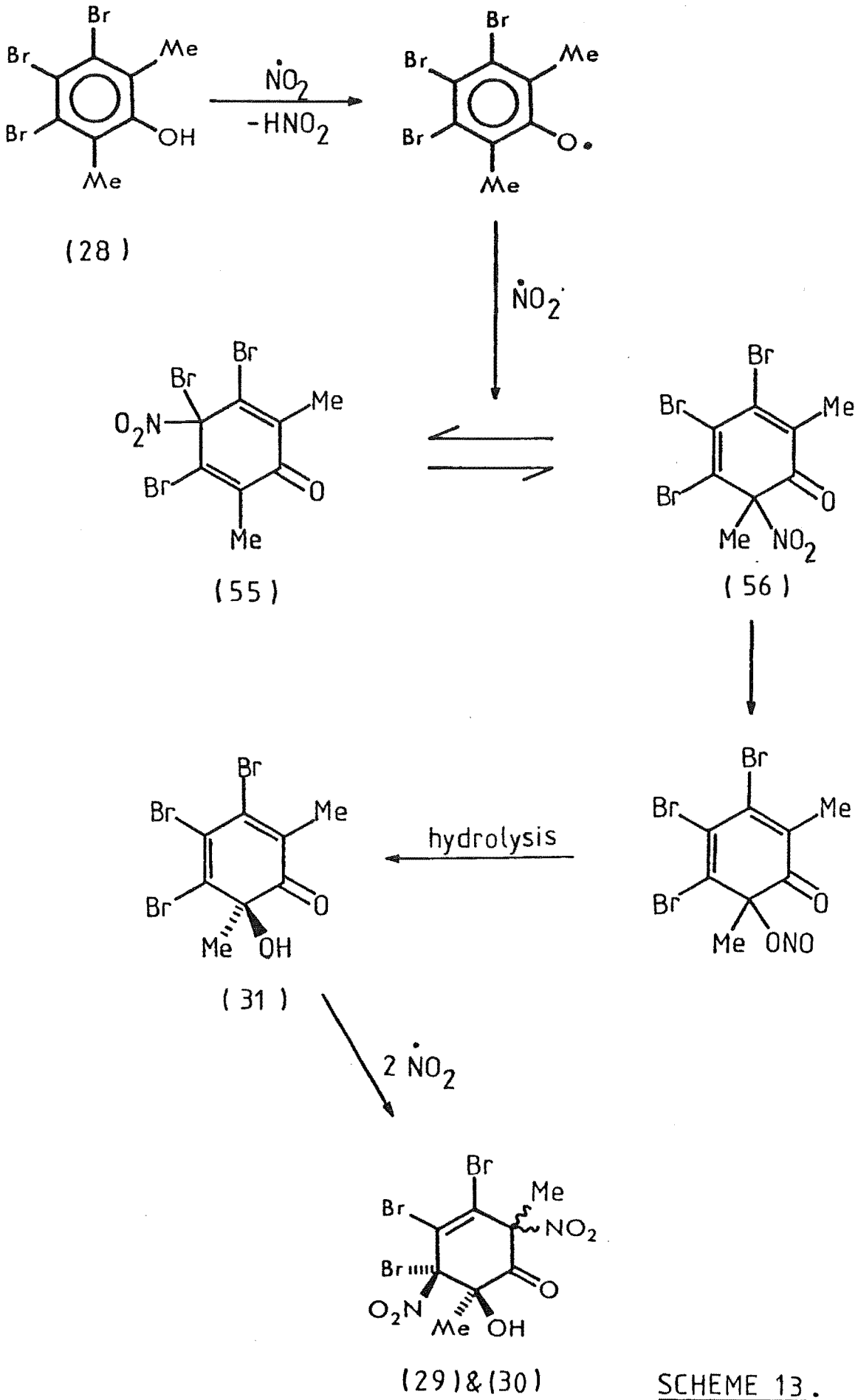
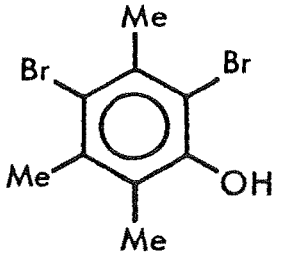


FIGURE 4.

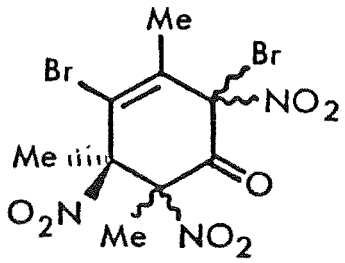

Br
Br
Me
Br
OH
Me
$\dot{N}O_2$
$-HNO_2$
Br
Br
Me
O•
Me
(28)
$\dot{N}O_2$
Br
Br
O_2N
Me
Br
O
Me
(55)
Br
Br
Me
Br
O
Me
NO_2
(56)
Br
Br
Me
Br
O
Me
ONO
hydrolysis
Br
Br
Me
Br
O
Me
OH
(31)
$2\,\dot{N}O_2$
Br
Br
Me
NO_2
Br
O_2N
O
Me
OH
(29)&(30)

SCHEME 13.

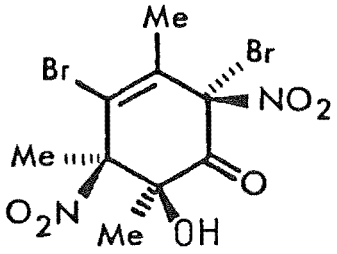
BLOCK F.



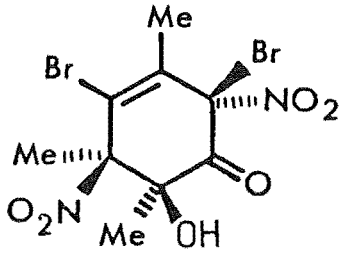
(57)



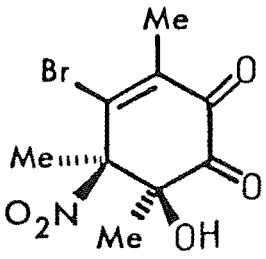
(58a) isolated isomer
(58b) other isomer(s)



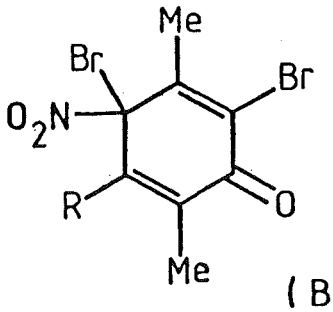
(59)



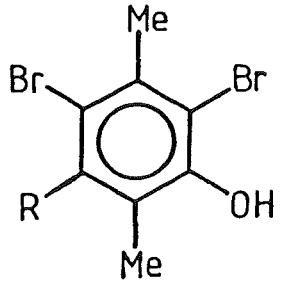
(60)



(61)

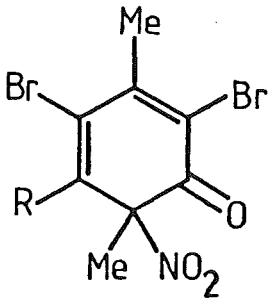


(B)

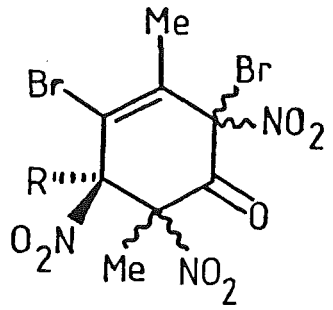


(A)

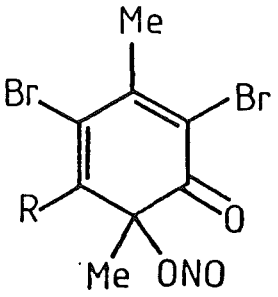
(5) R=Br
(57) R=Me



(C)

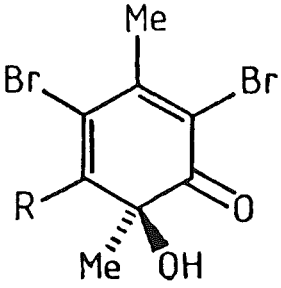


(F)

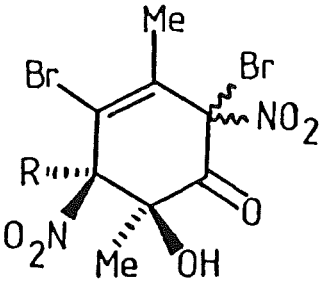


(D)

hydrolysis

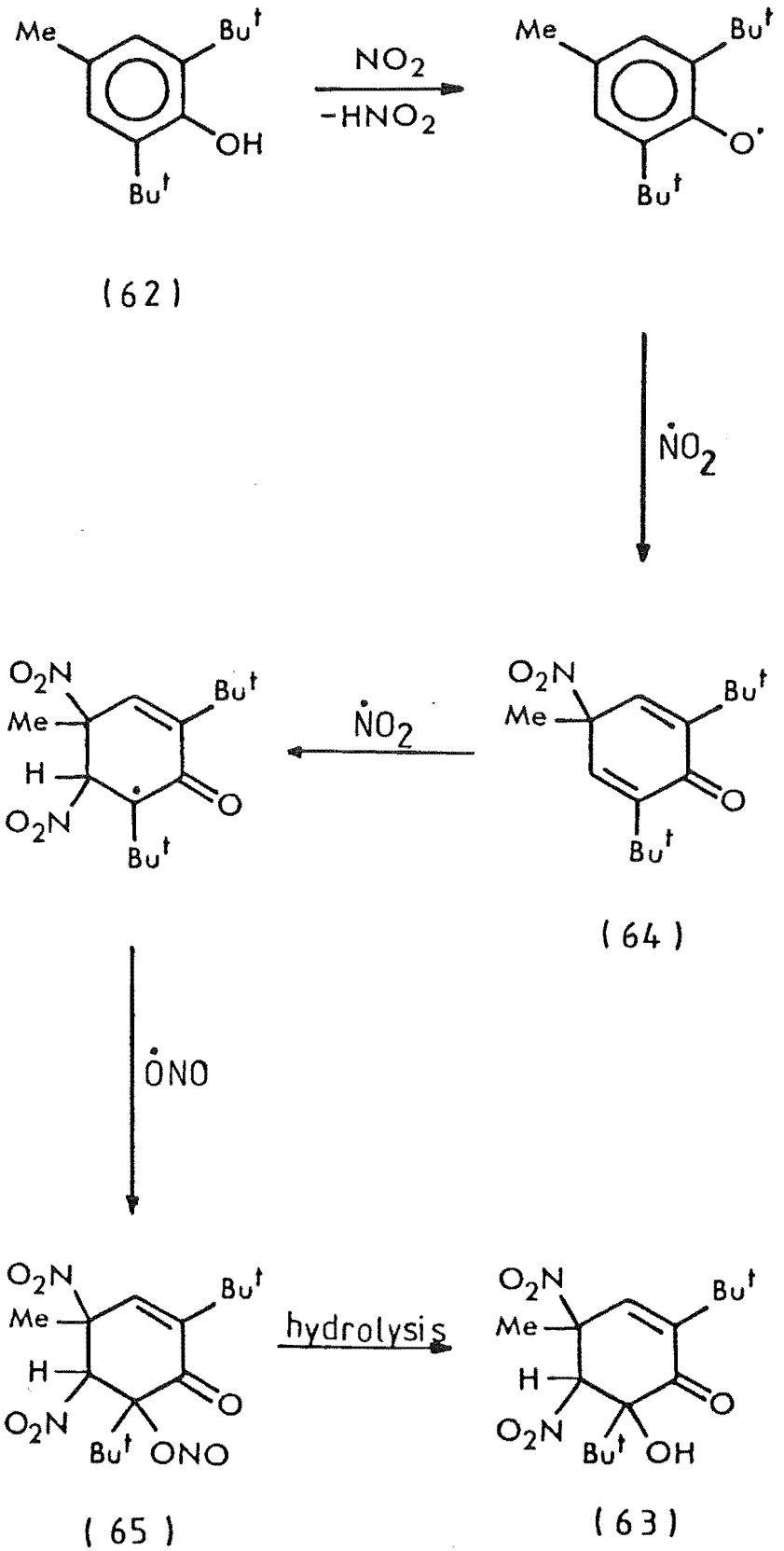


(E)



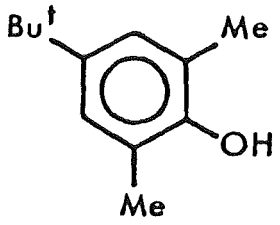
(G)

SCHEME 14.


Me
Bu^t
OH
Bu^t
NO_2
$-HNO_2$
Me
Bu^t
O$^\cdot$
Bu^t
(62)
$\dot{N}O_2$
O_2N
Me
H
O_2N
Bu^t
O
Bu^t
$\dot{N}O_2$
O_2N
Me
Bu^t
O
Bu^t
(64)
$\dot{O}NO$
O_2N
Me
H
O_2N
Bu^t
O
Bu^t ONO
hydrolysis
O_2N
Me
H
O_2N
Bu^t
O
Bu^t OH
(65)
(63)

SCHEME 15.

BLOCK G.



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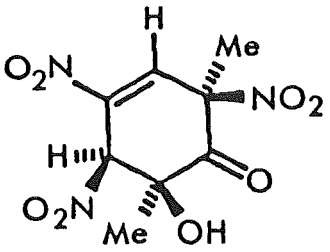

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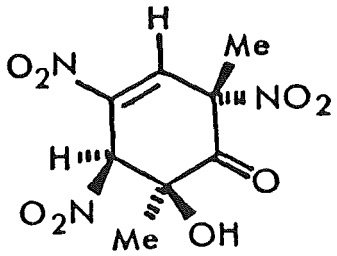

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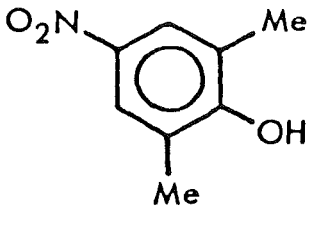

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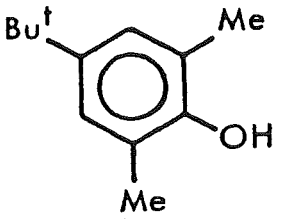

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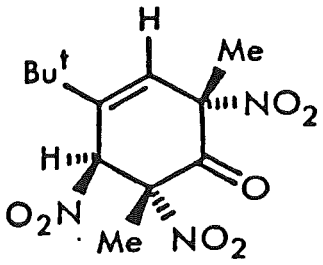

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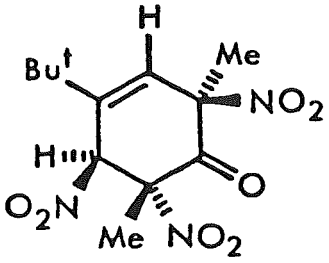

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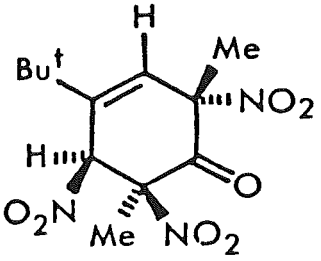
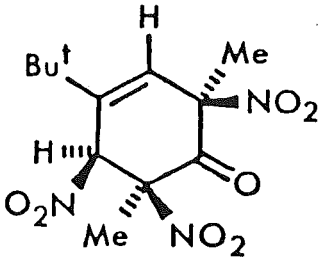


(72)



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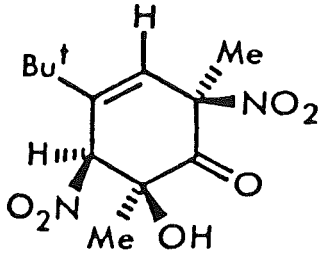
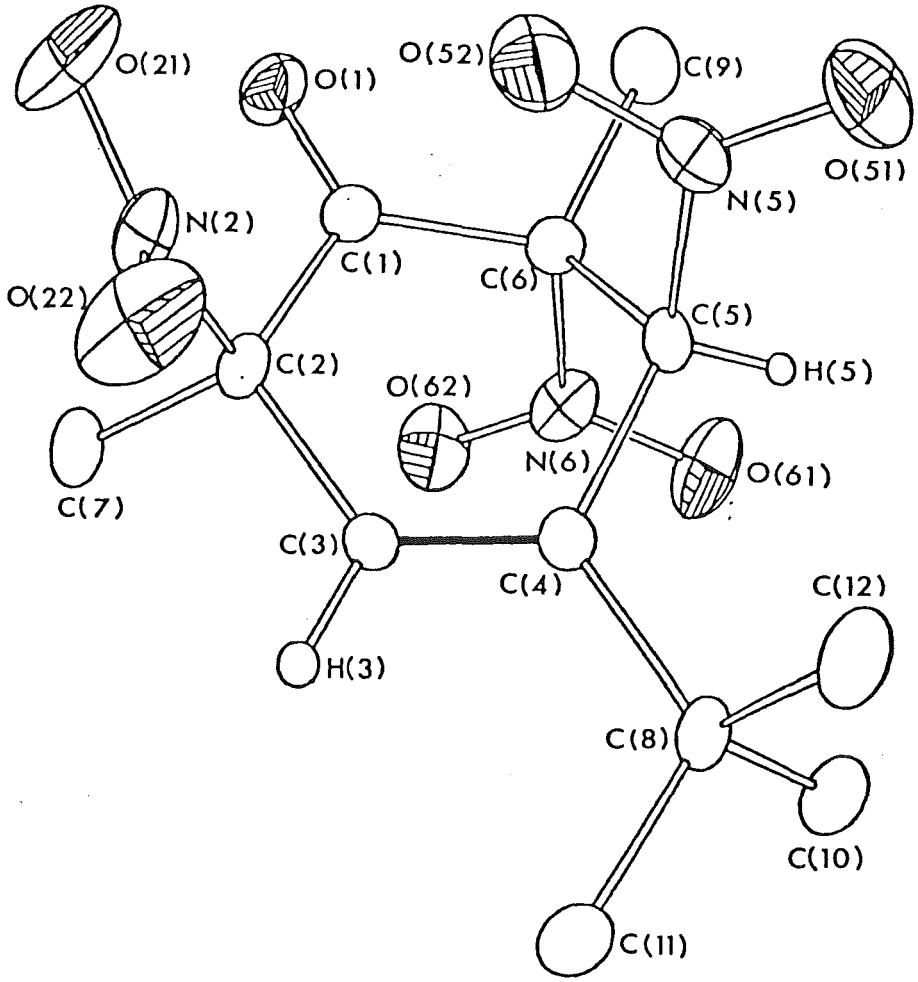
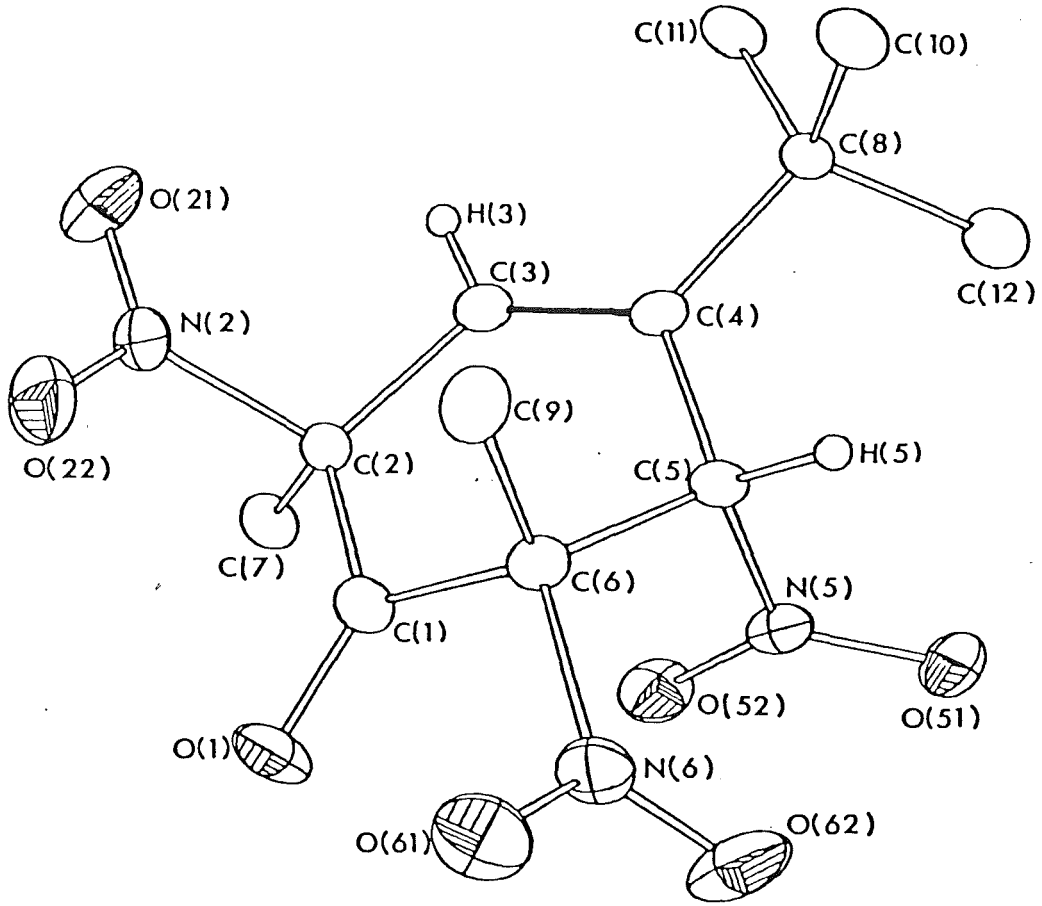


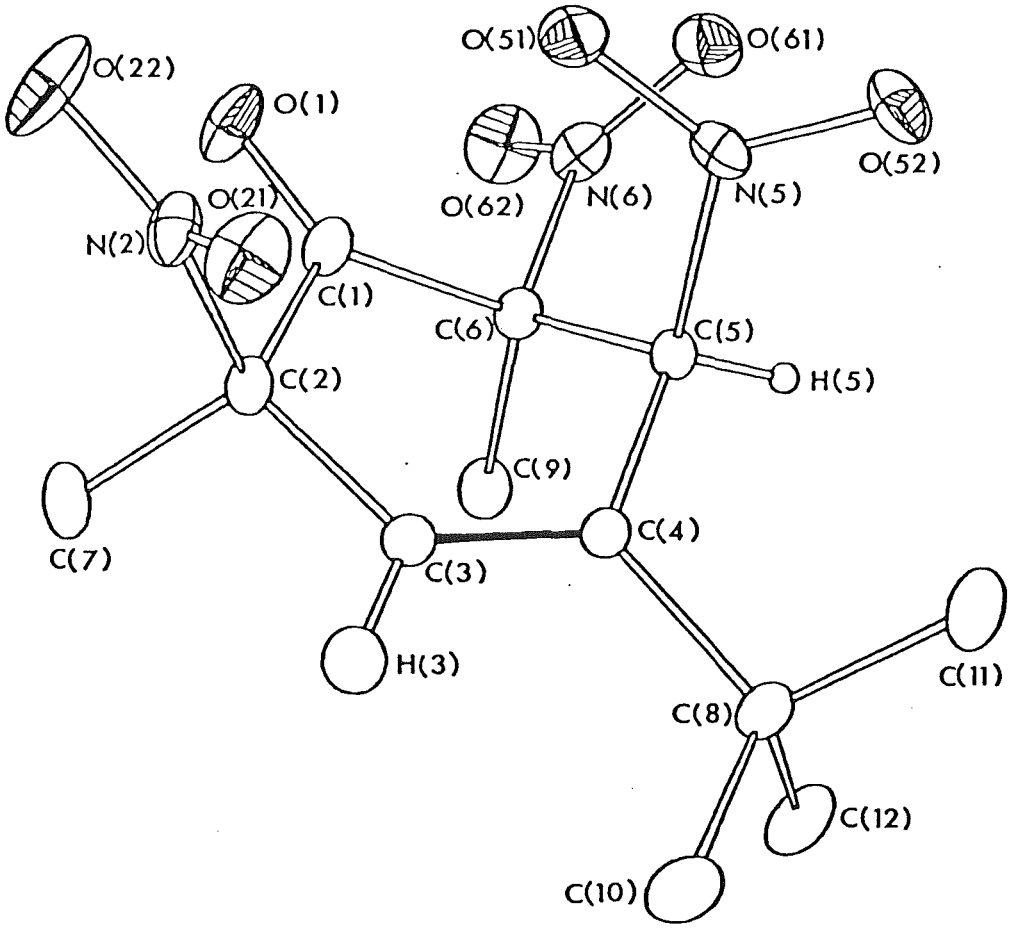
(74)



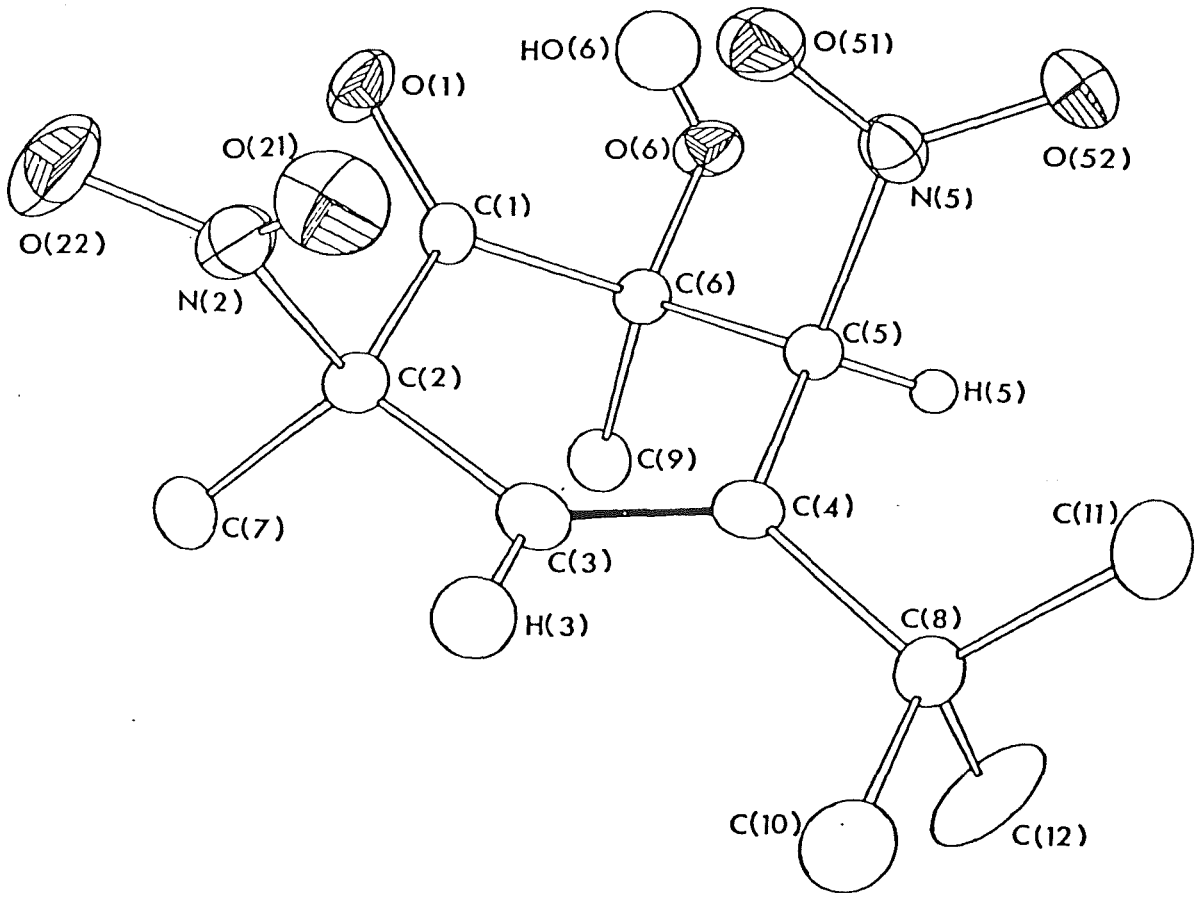
(71) FIGURE 5.



(72) FIGURE 6.



(73) FIGURE 7.



(74) FIGURE 8.

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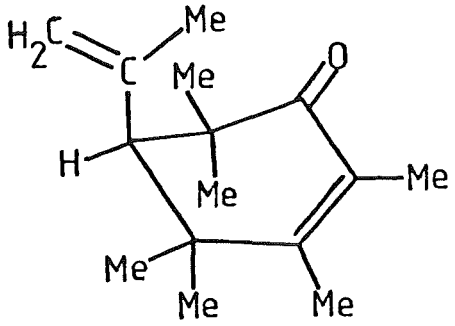

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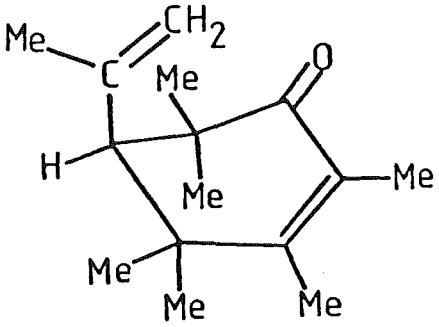

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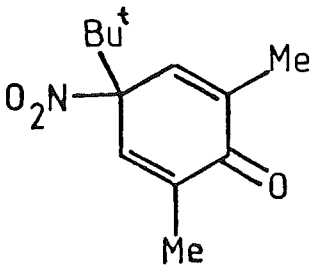

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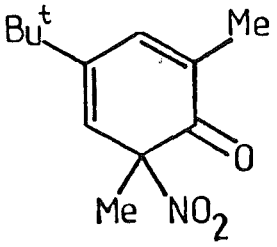

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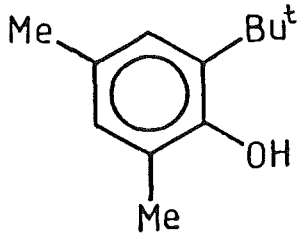

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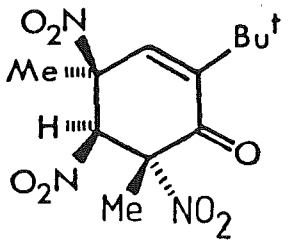

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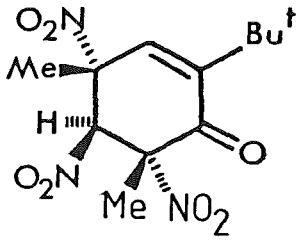

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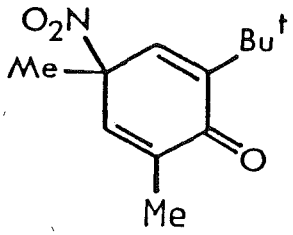

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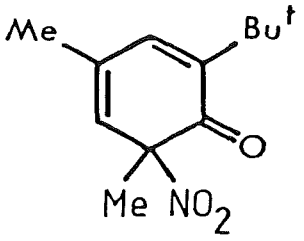

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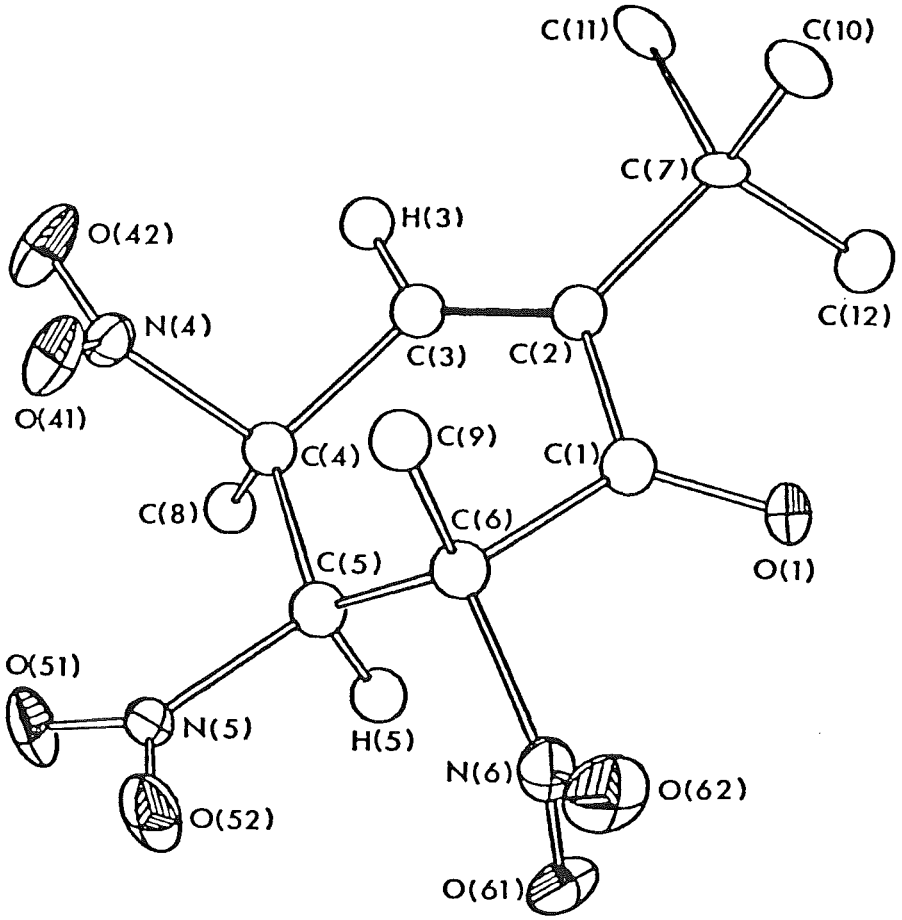

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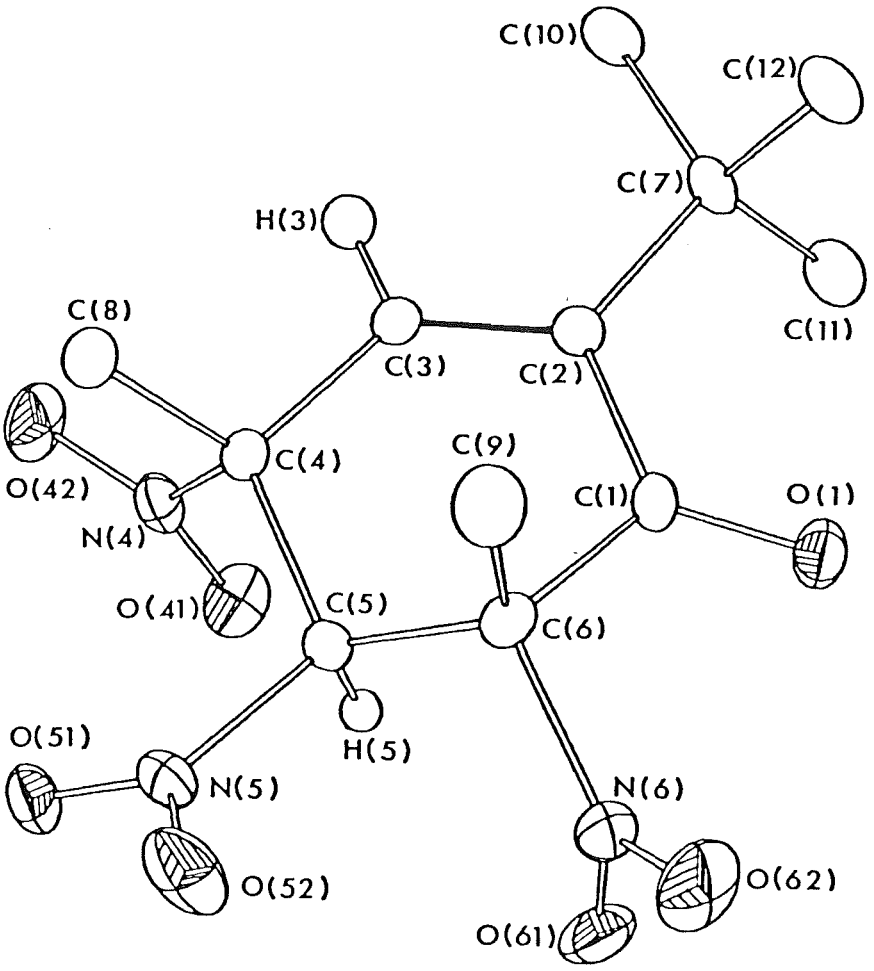
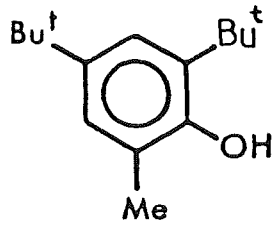
FIGURE 9.



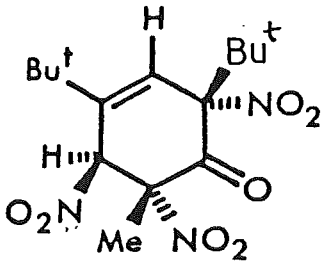
(81)

FIGURE 10.

BLOCK K.



(84)



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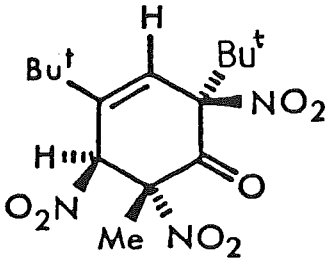

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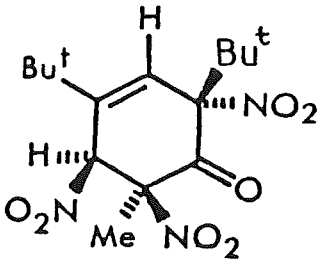

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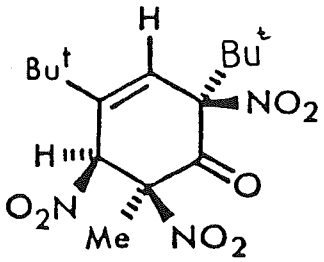

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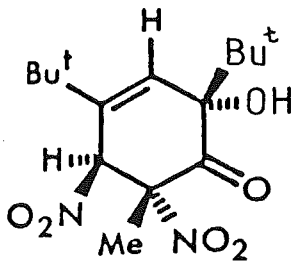

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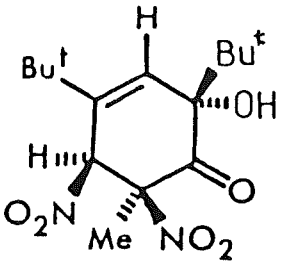

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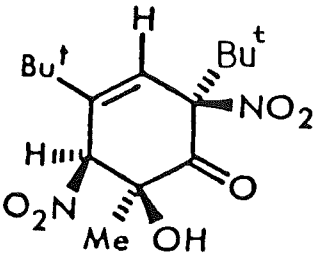
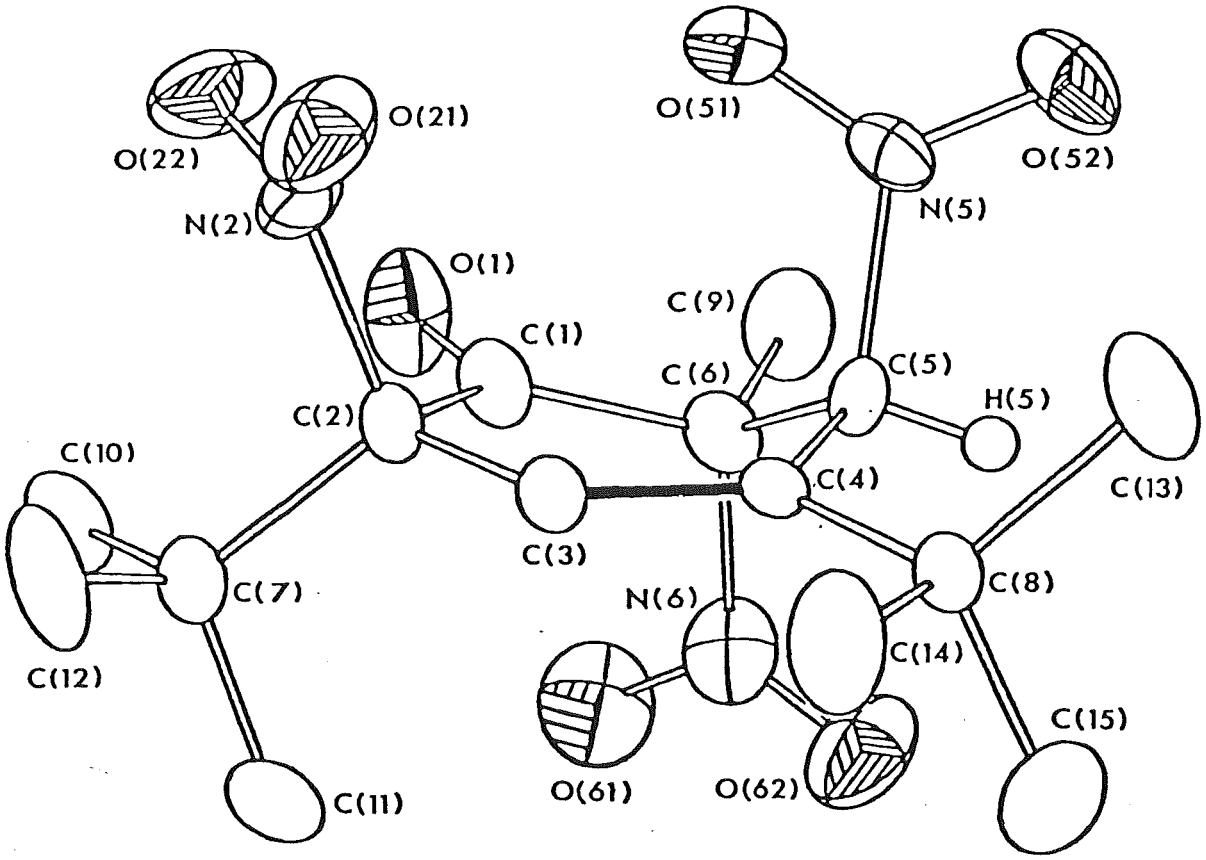
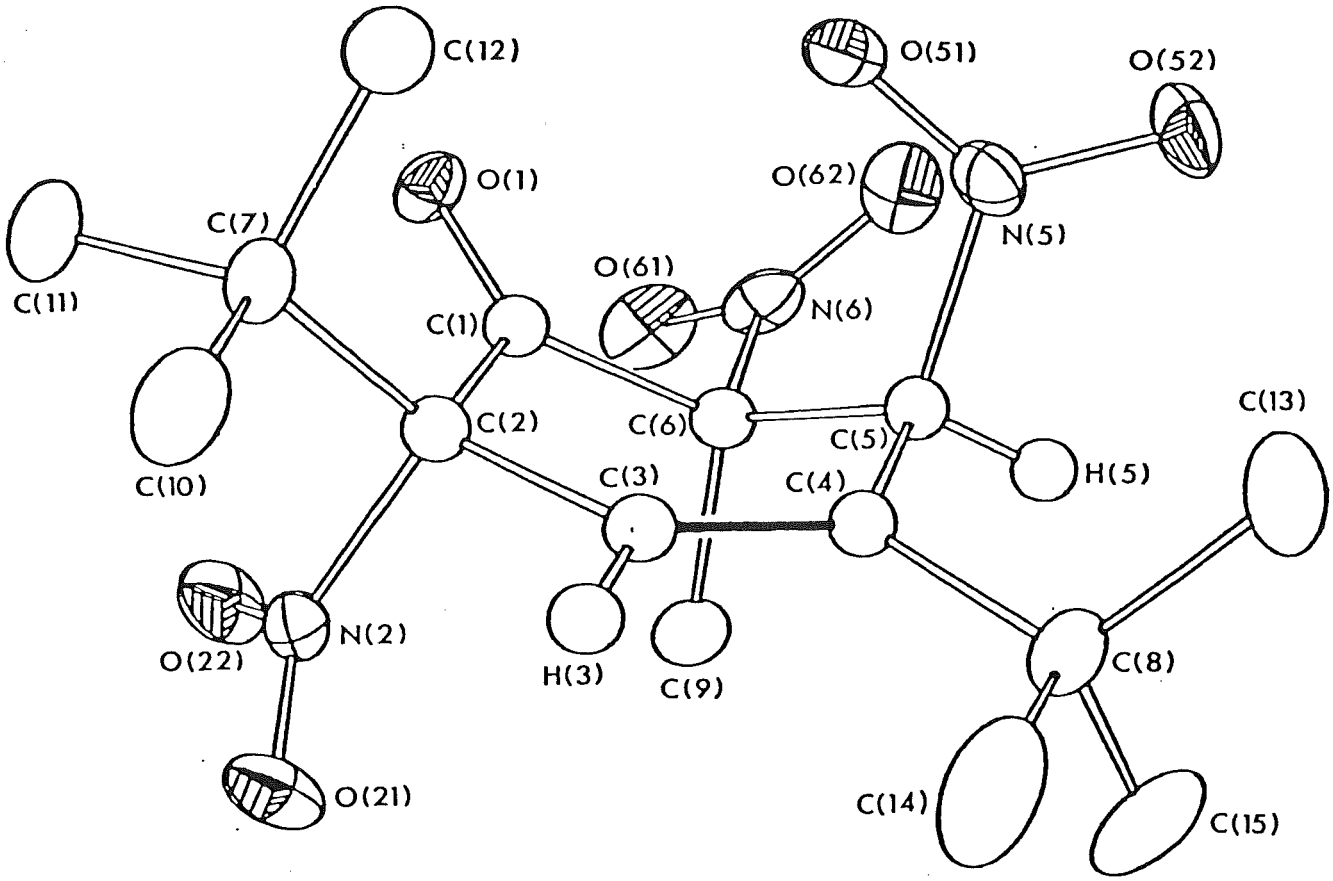


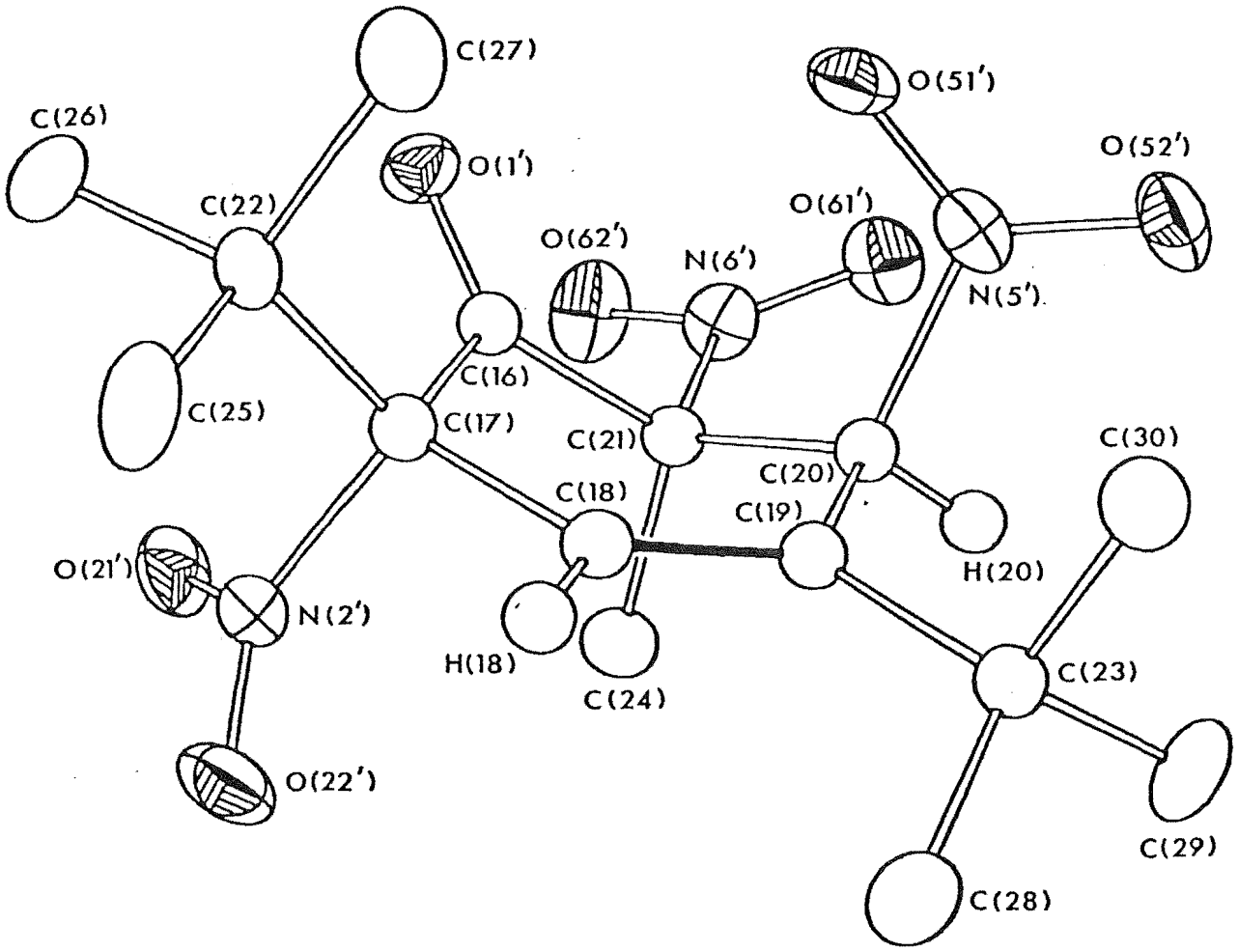
(91)



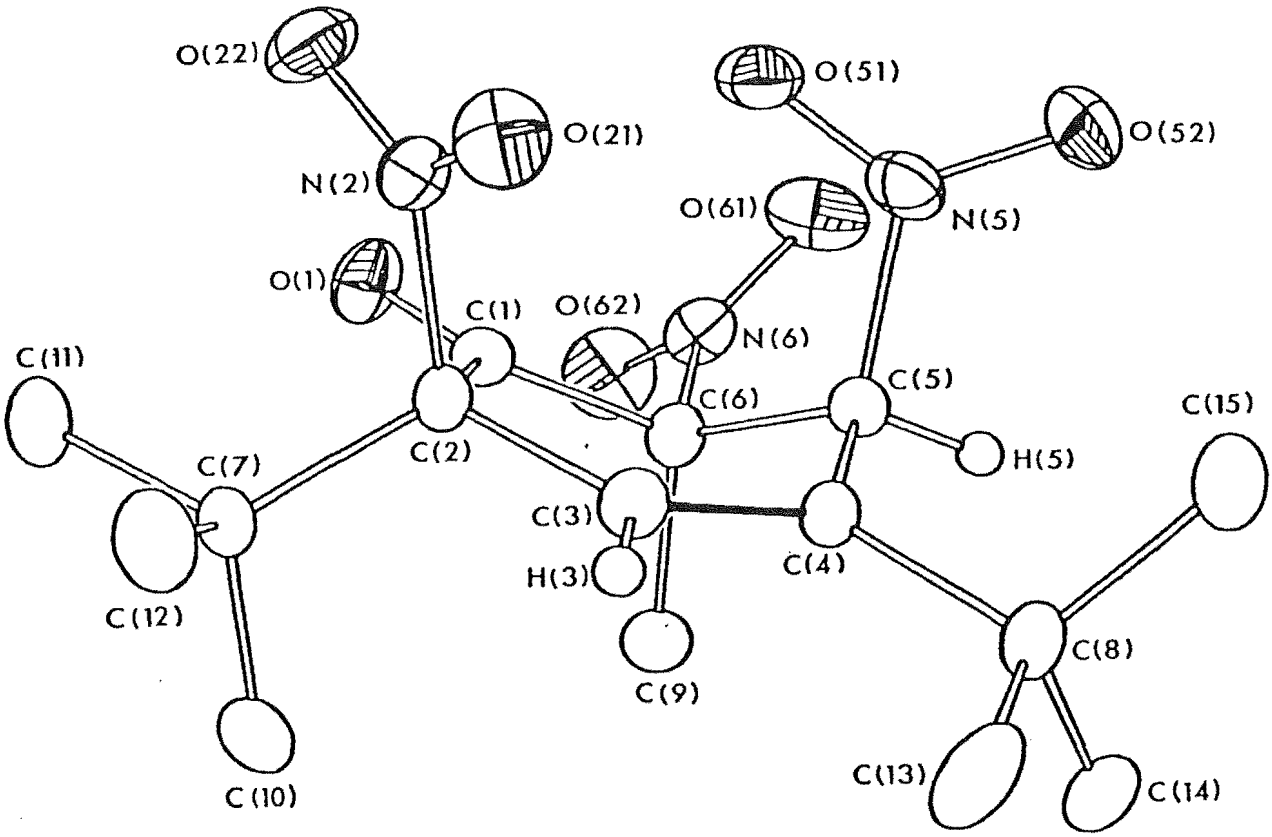
(86) FIGURE 11.



(87) (molecule one) FIGURE 12.



(87)(molecule two) FIGURE 13.



(88) FIGURE 14.

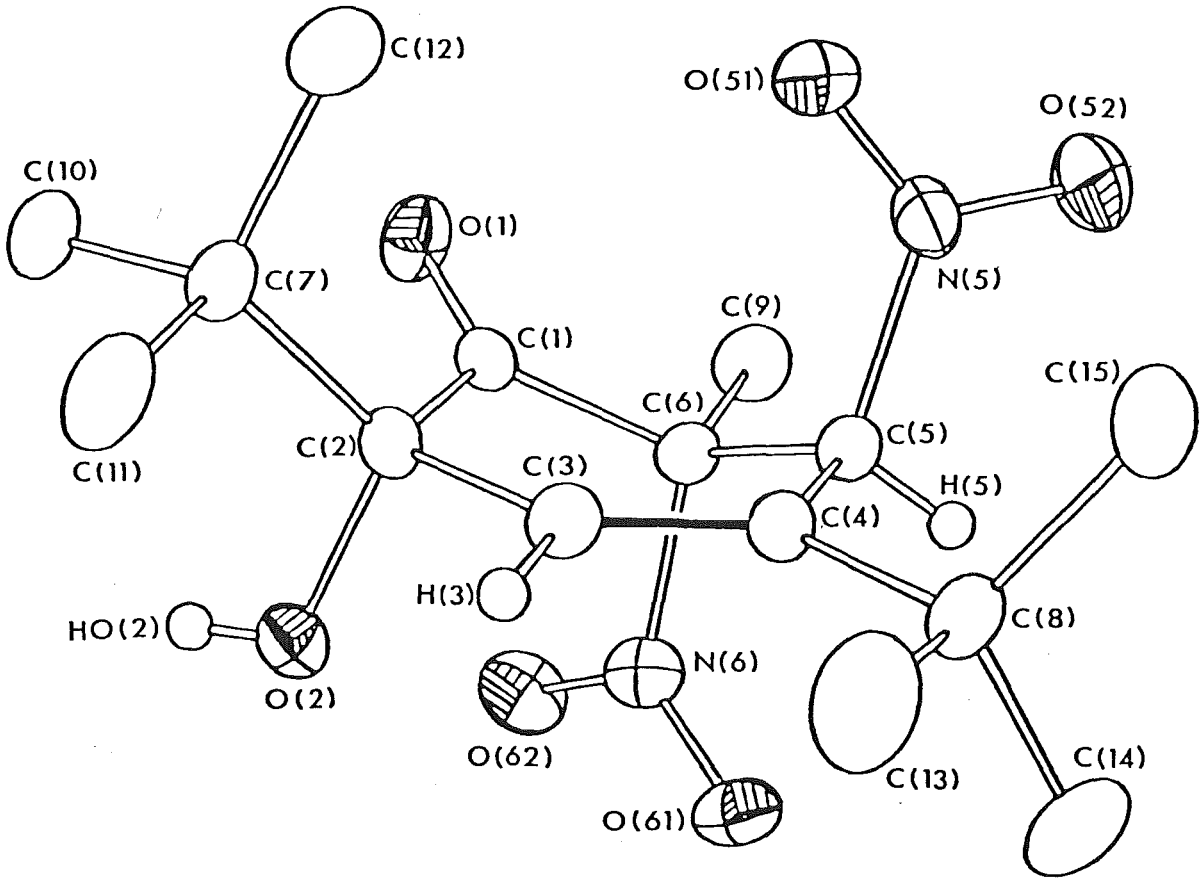


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FIGURE 15.

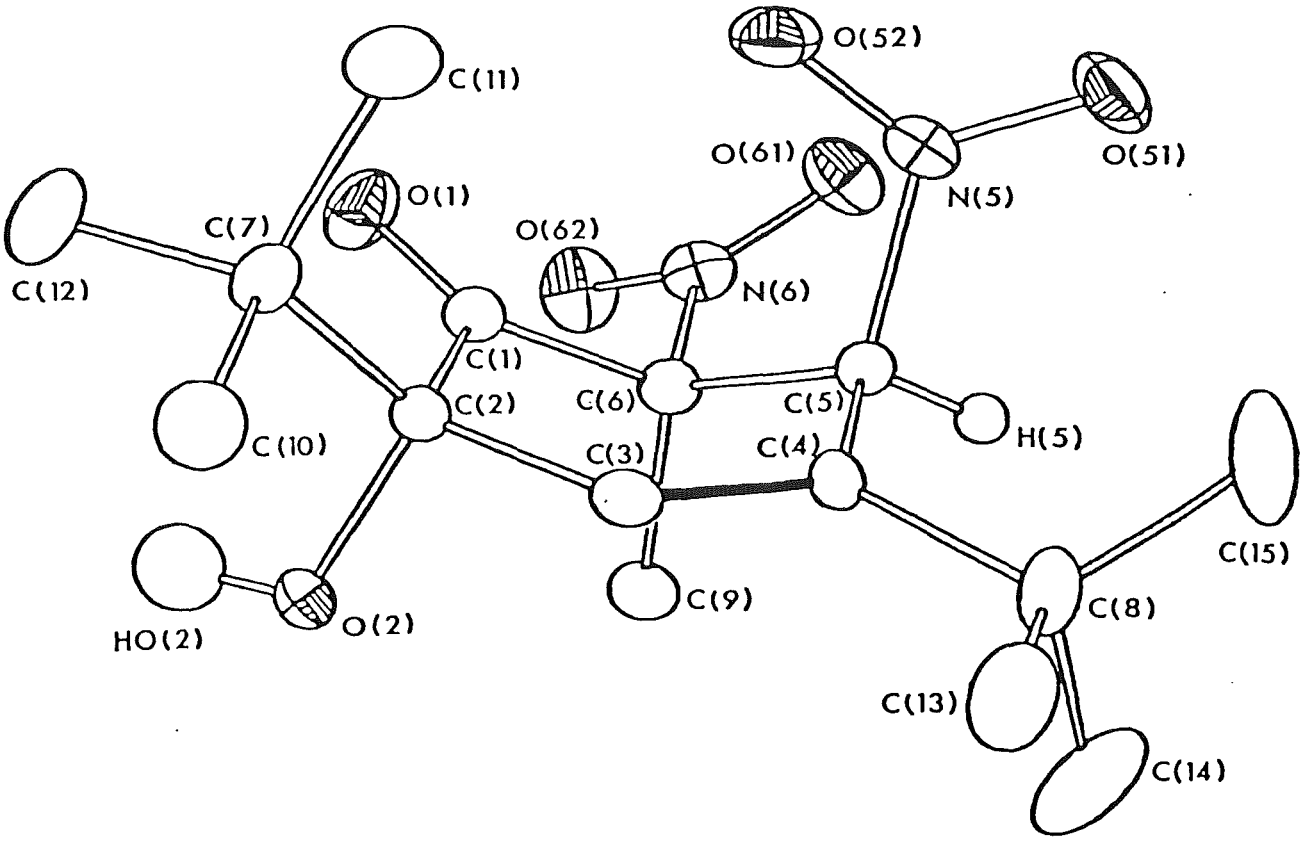

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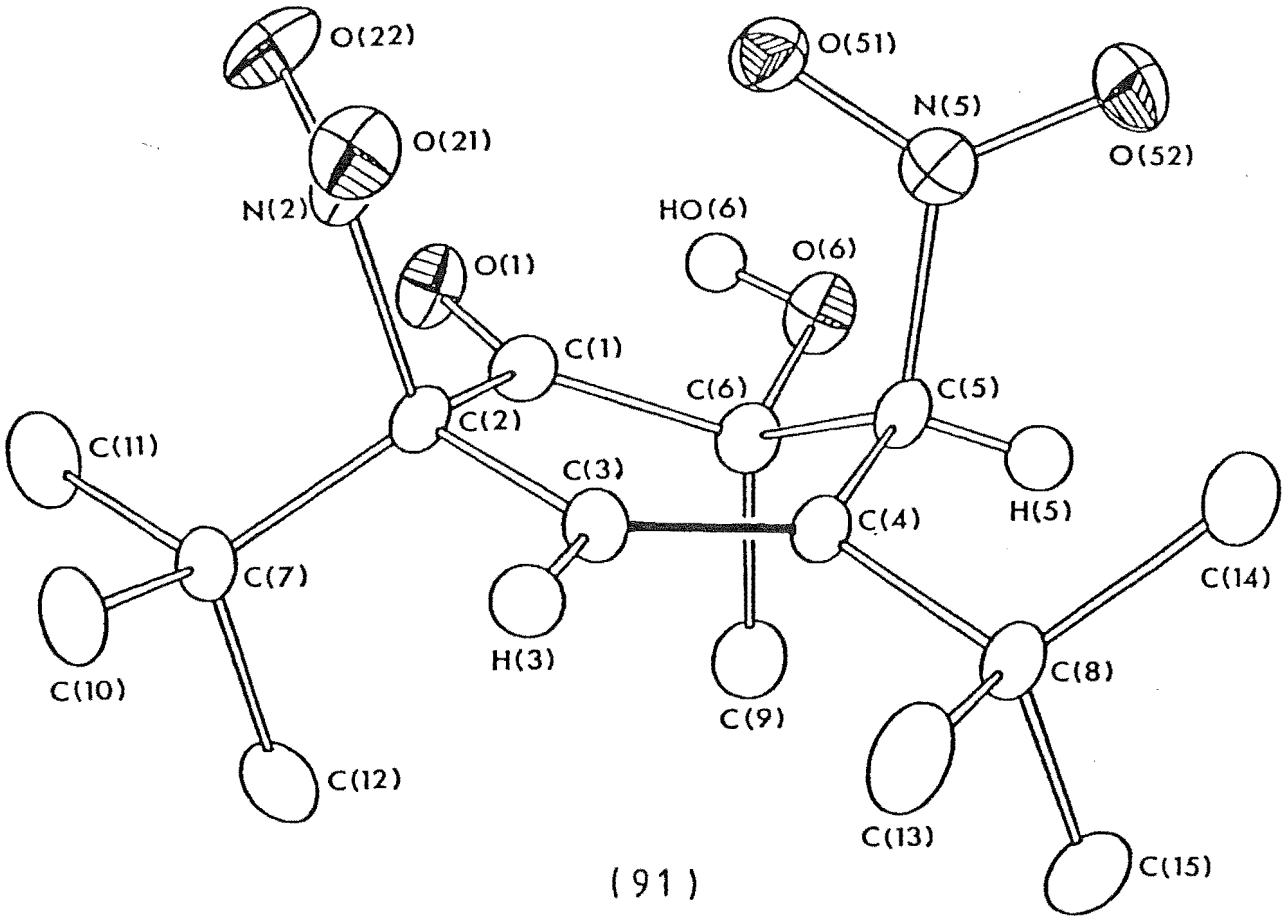
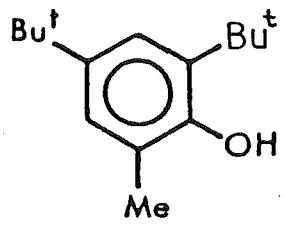
FIGURE 16.


O(22)
O(21)
N(2)
O(1)
C(1)
C(2)
C(11)
C(7)
C(10)
C(12)
C(3)
H(3)
HO(6)
O(6)
C(6)
C(9)
O(51)
N(5)
O(52)
C(5)
H(5)
C(4)
C(14)
C(8)
C(13)
C(15)

(91)

FIGURE 17.

BLOCK L.



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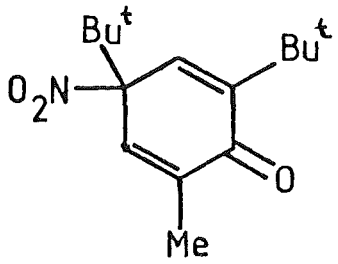

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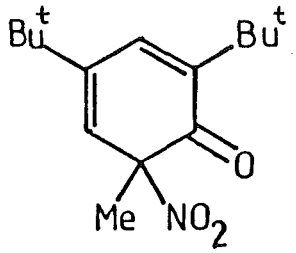

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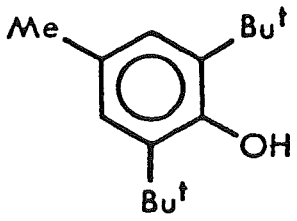
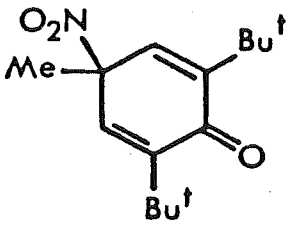
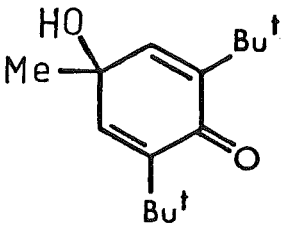


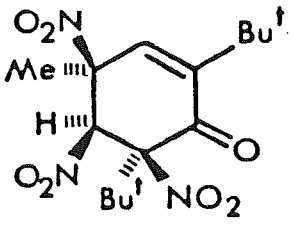
(62)



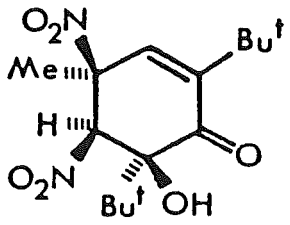
(64)



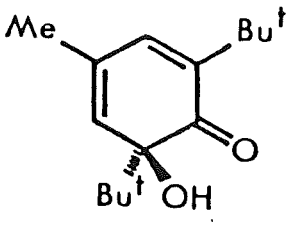
(94)



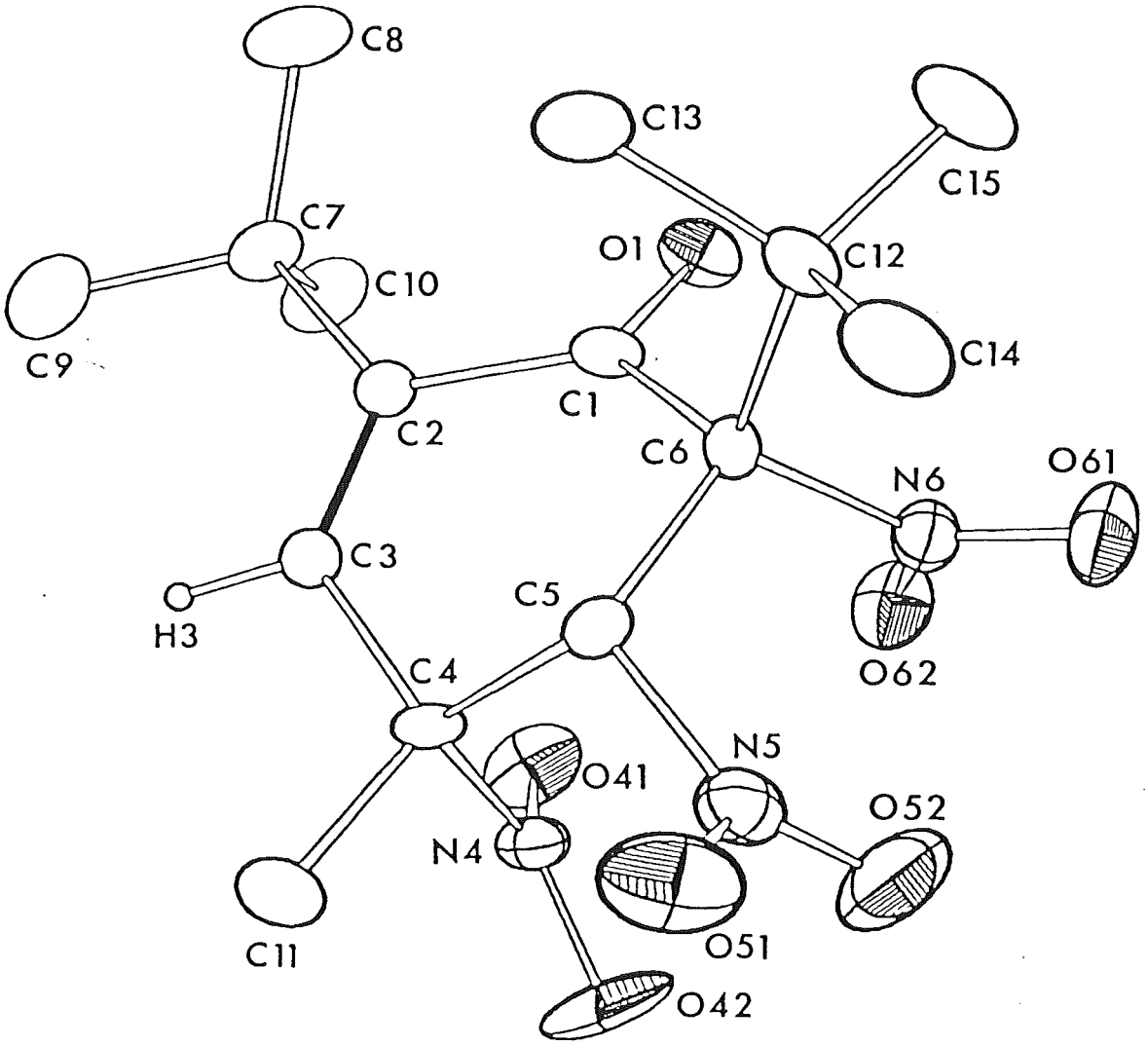
(95)



(96)

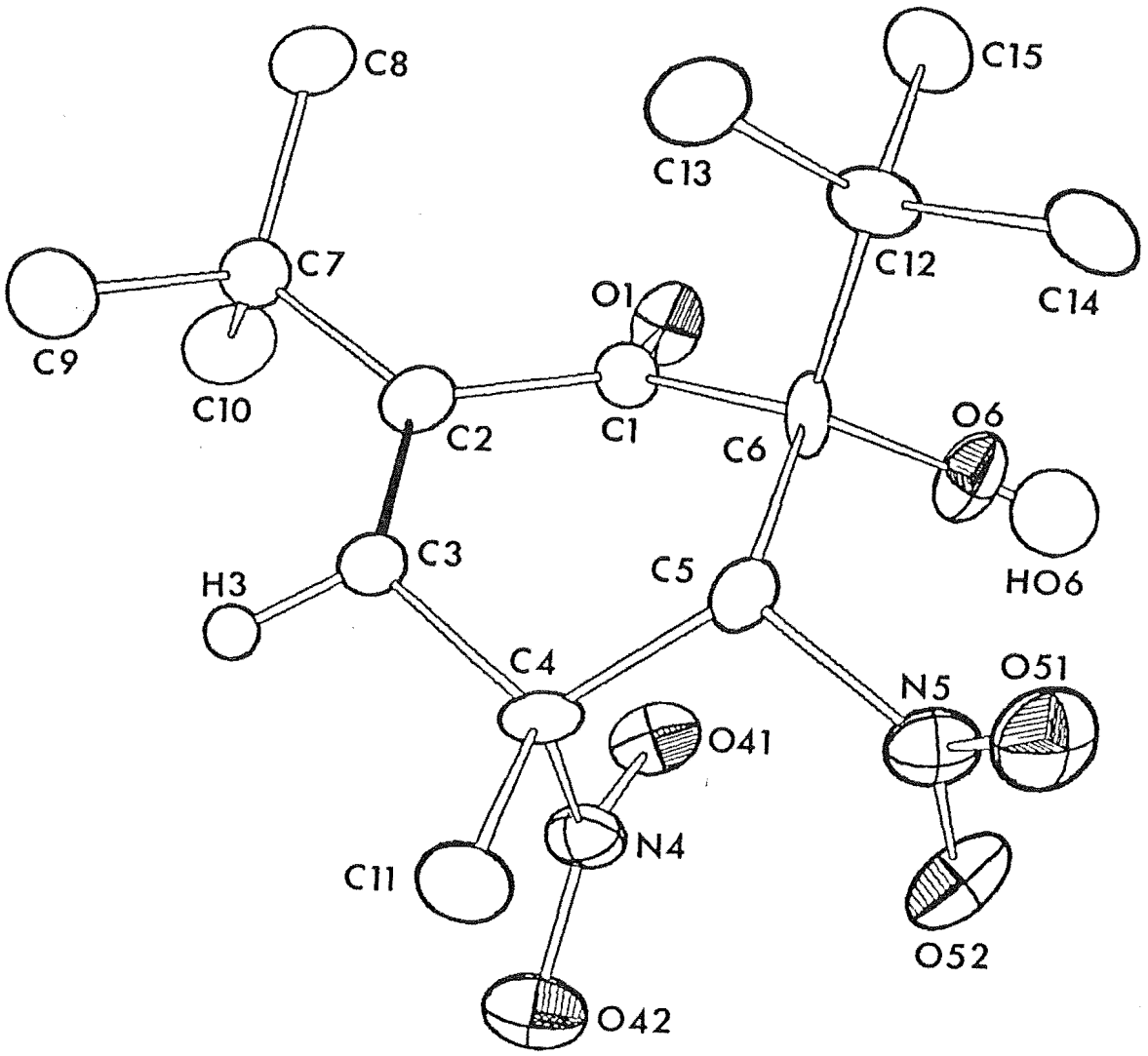


(97)


C8
C13
C15
C7
O1
C12
C10
C14
C9
C1
C2
C6
O61
N6
C3
C5
H3
O62
C4
N5
O41
O52
N4
C11
O51
O42

(95)

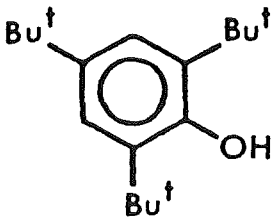
FIGURE 18.


C8
C15
C13
C7
C12
C14
O1
C9
C10
C2
C1
C6
O6
C3
C5
H3
HO6
C4
O51
N5
O41
N4
C11
O52
O42

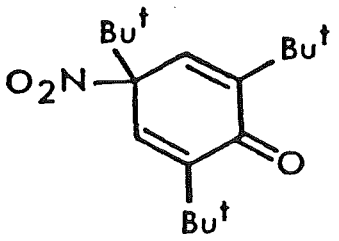
(96)

FIGURE 19.

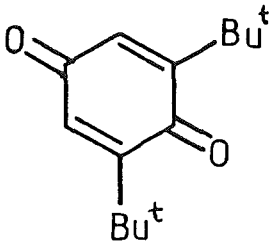
BLOCK N.



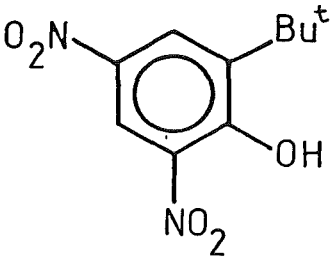
(98)



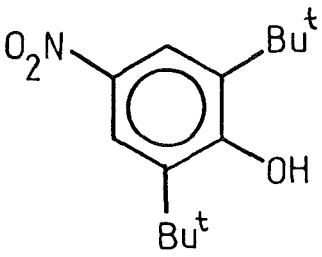
(99)



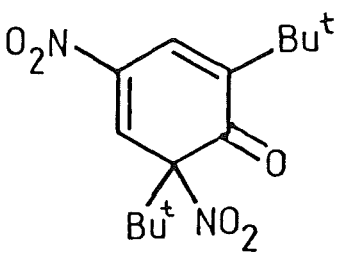
(100)



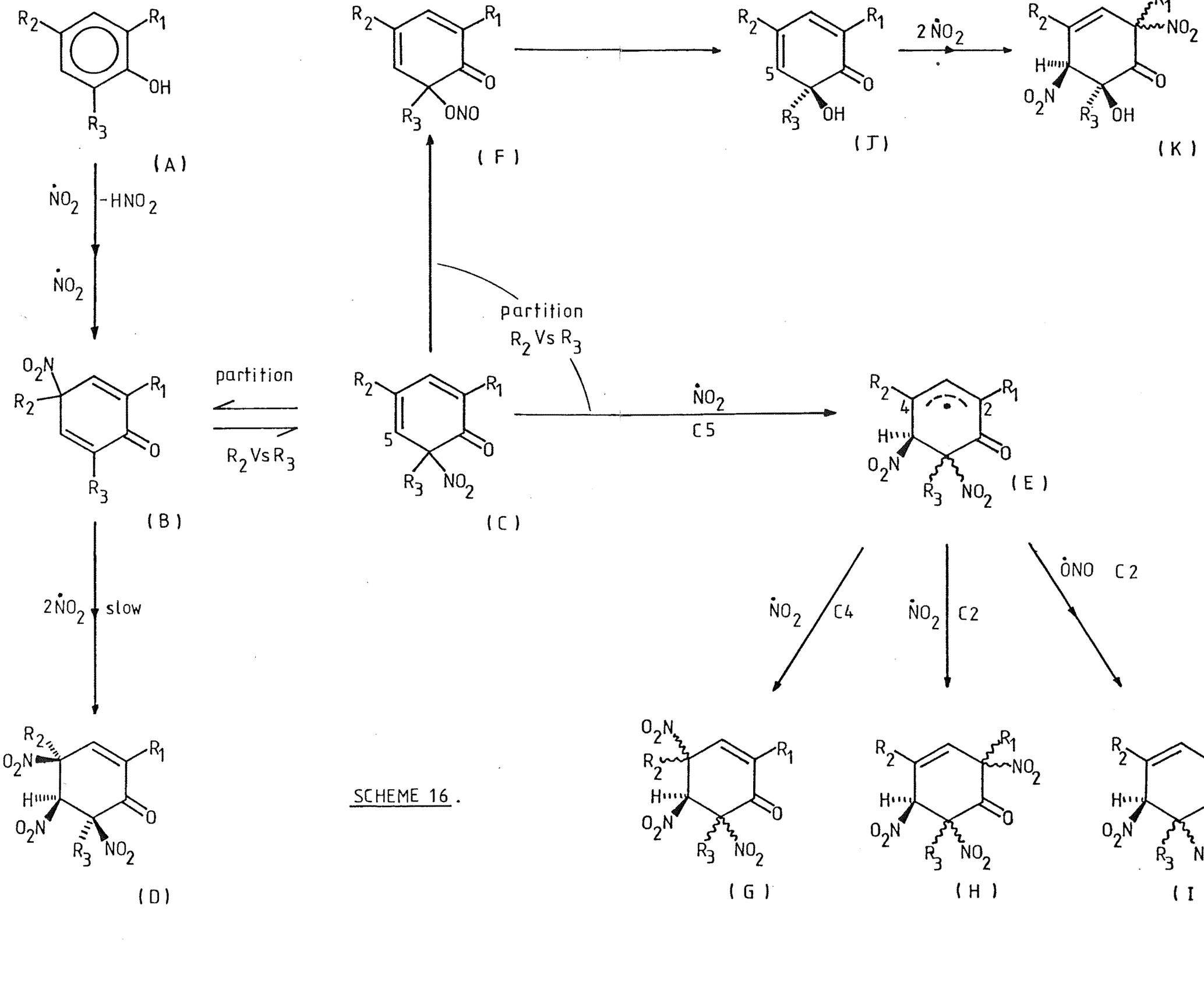
(101)



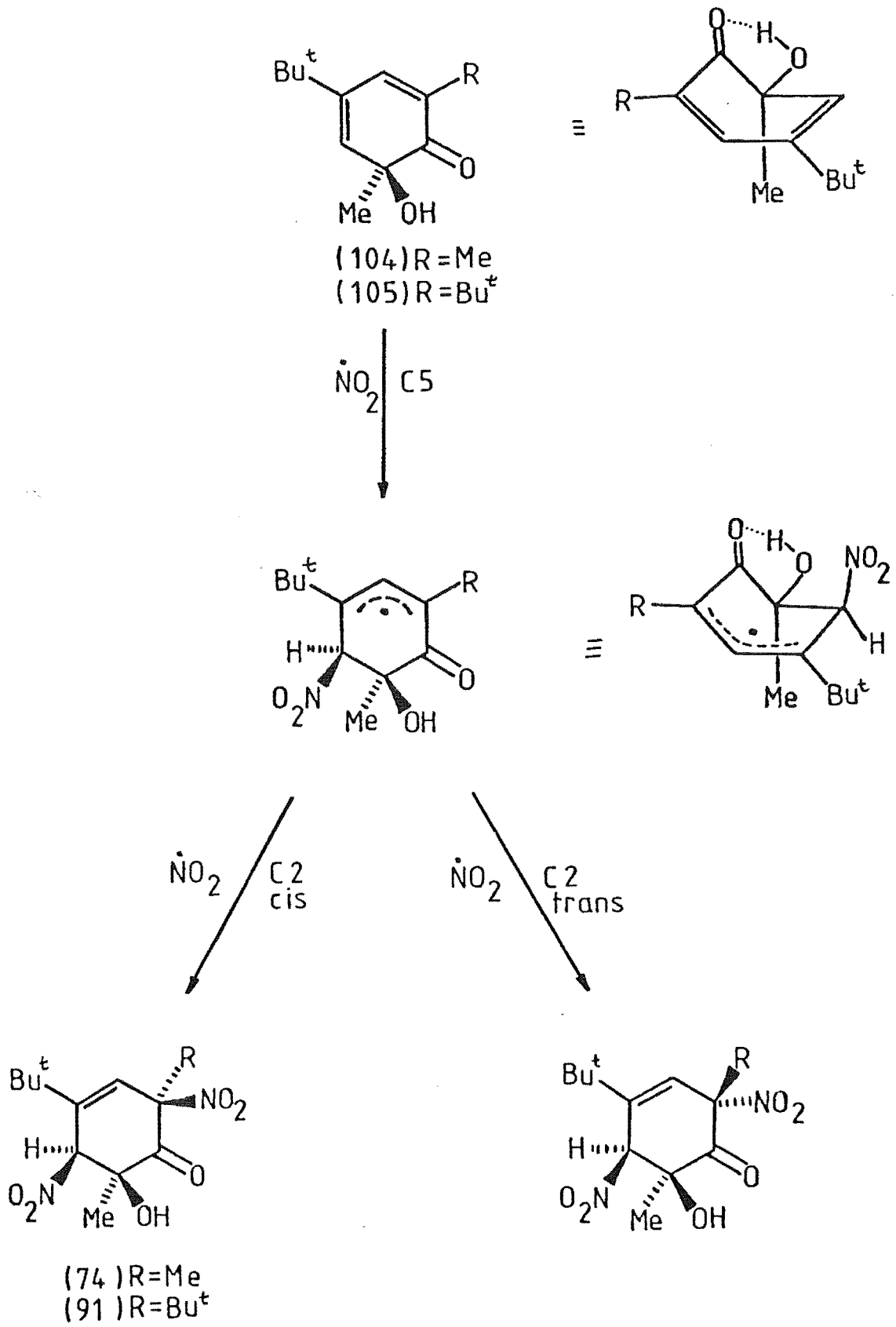
(102)



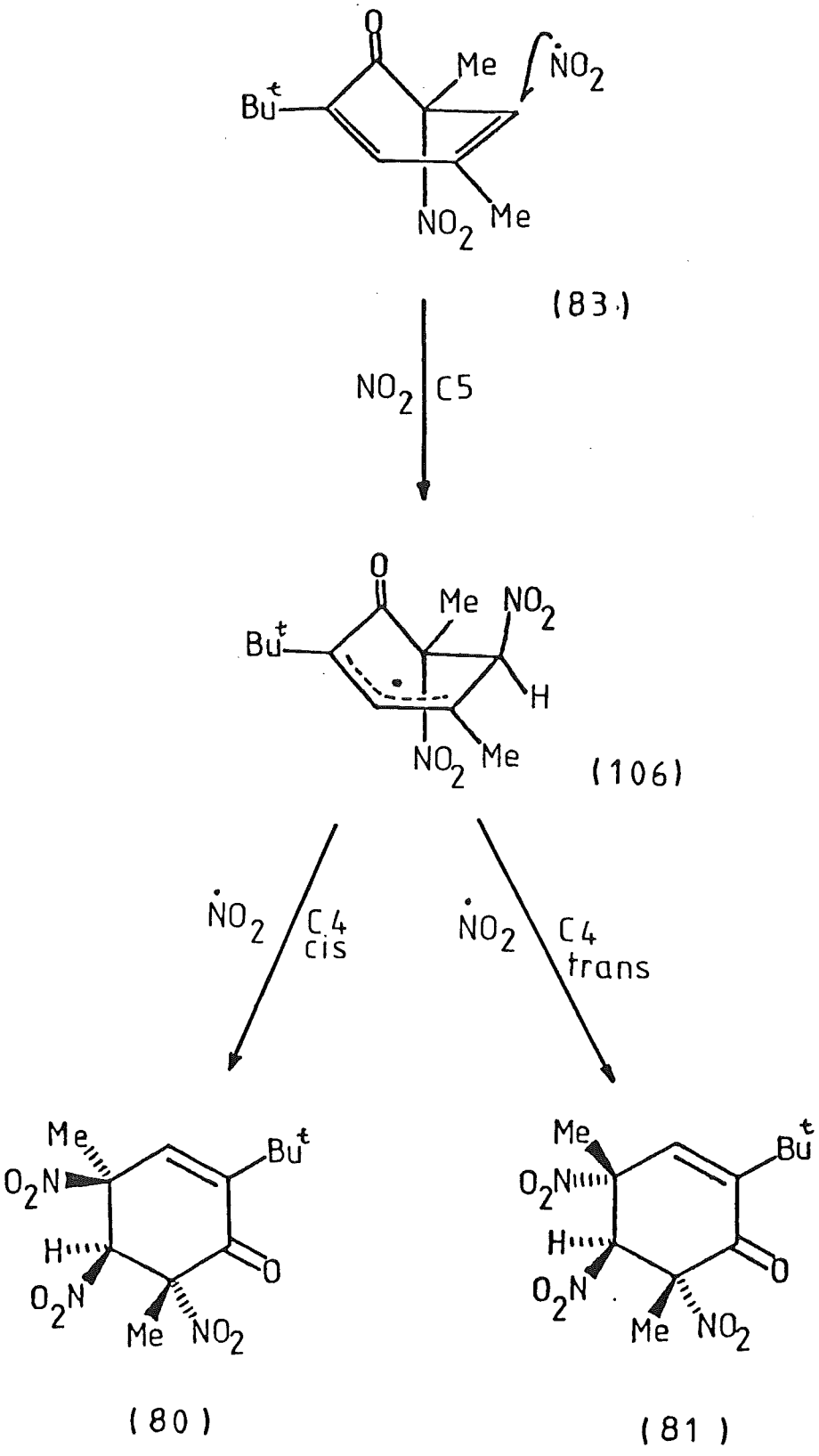
(103)


(A)
$\dot{N}O_2$ -HNO_2
$\dot{N}O_2$
partition
R_2 Vs R_3
R_2 Vs R_3
(B)
(C)
(F)
partition
R_2 Vs R_3
$\dot{N}O_2$
C5
(J)
$2\dot{N}O_2$
(K)
(E)
$2\dot{N}O_2$ slow
$\dot{N}O_2$ C4
$\dot{N}O_2$ C2
$\dot{O}NO$ C2
(D)
(G)
(H)
(I)

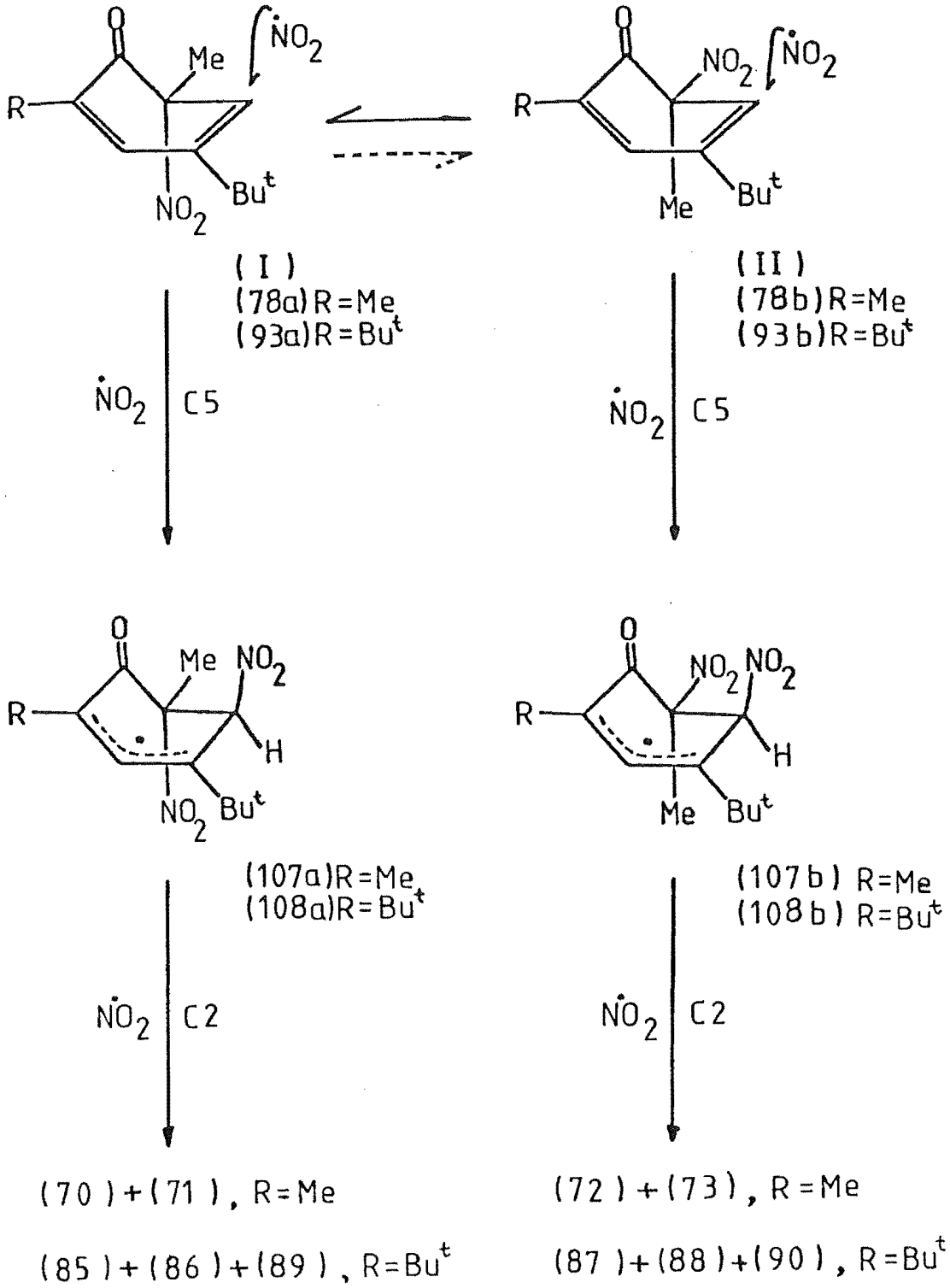
SCHEME 16.


Bu^t
R
O
Me
OH
≡
O···H
O
R
Me
Bu^t
(104) R = Me
(105) R = Bu^t
ṄO2
C5
H
O2N
NO2
H
C2
cis
C2
trans
(74) R = Me
(91) R = Bu^t

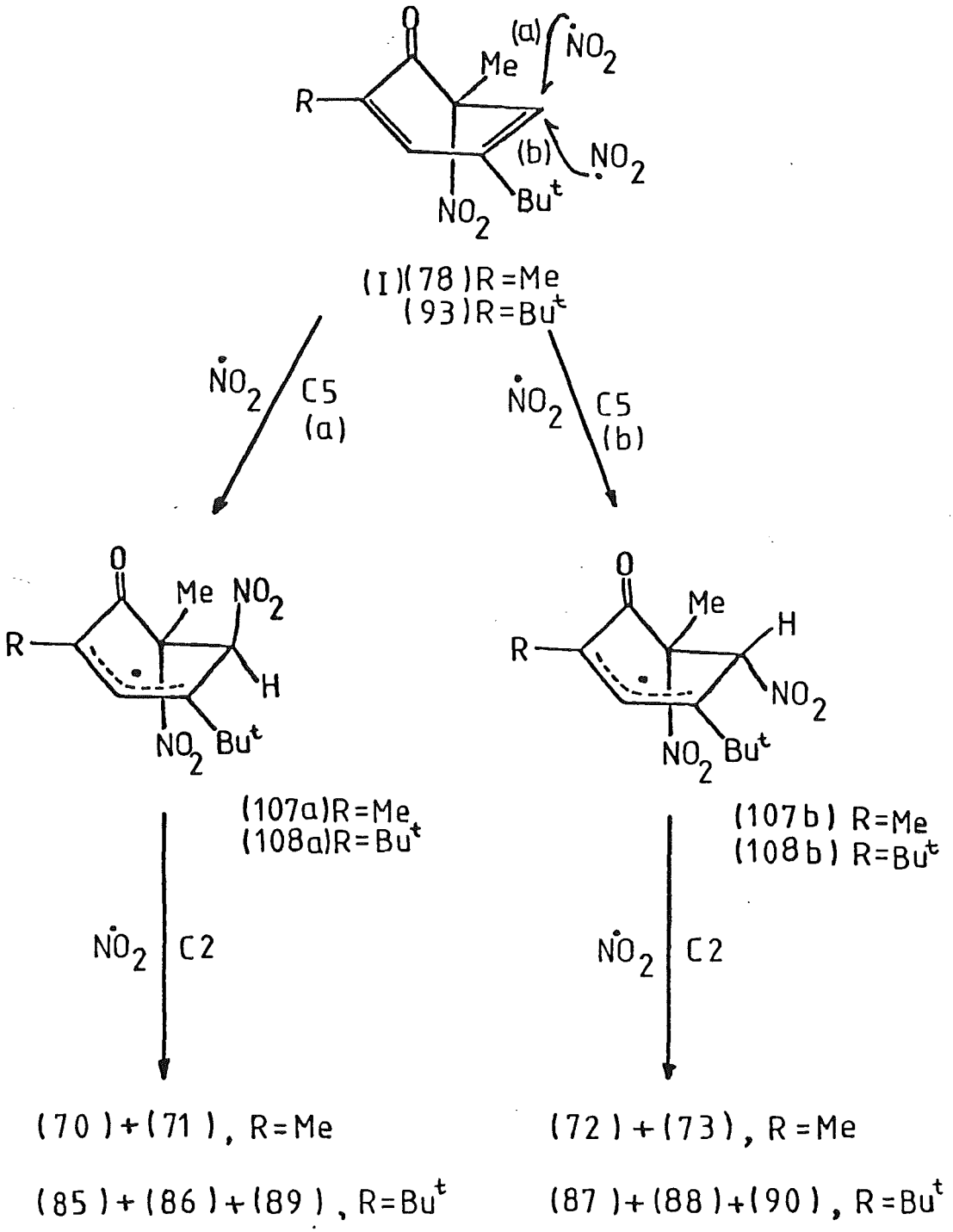
SCHEME 17 .


O
Me
$\dot{N}O_2$
Bu^t
NO_2
Me
(83)
NO_2 C5
O
Me
NO_2
Bu^t
H
NO_2
Me
(106)
$\dot{N}O_2$ C4 cis
$\dot{N}O_2$ C4 trans
Me
Bu^t
O_2N
H
O_2N
O
Me
NO_2
(80)
Me
Bu^t
O_2N
H
O_2N
O
Me
NO_2
(81)

SCHEME 18 .

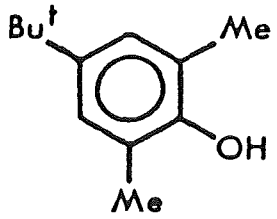

R
Me
$\dot{N}O_2$
NO_2
Bu^t
(I)
(78a) R=Me
(93a) R=Bu^t
$\dot{N}O_2$ C5
NO_2
Me
Bu^t
(II)
(78b) R=Me
(93b) R=Bu^t
$\dot{N}O_2$ C5
H
(107a) R=Me
(108a) R=Bu^t
$\dot{N}O_2$ C2
(107b) R=Me
(108b) R=Bu^t
$\dot{N}O_2$ C2
(70) + (71), R=Me
(85) + (86) + (89), R=Bu^t
(72) + (73), R=Me
(87) + (88) + (90), R=Bu^t

SCHEME 19.

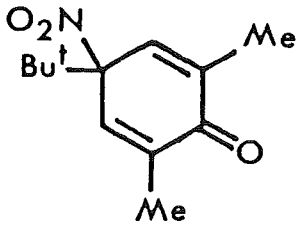

O
Me
(a) NO2
R
(b) NO2
NO2
Bu^t
(I)(78)R=Me
(93)R=Bu^t
NO2 C5 (a)
NO2 C5 (b)
O
Me NO2
R
H
NO2 Bu^t
(107a)R=Me
(108a)R=Bu^t
O
Me
H
R
NO2
NO2 Bu^t
(107b) R=Me
(108b) R=Bu^t
NO2 C2
NO2 C2
(70)+(71), R=Me
(85)+(86)+(89), R=Bu^t
(72)+(73), R=Me
(87)+(88)+(90), R=Bu^t

SCHEME 20.

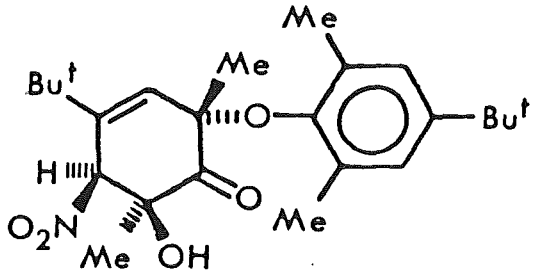
BLOCK O .



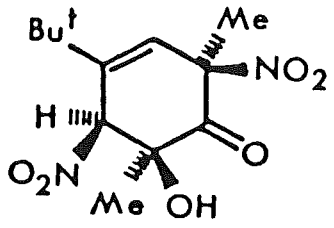
(66)



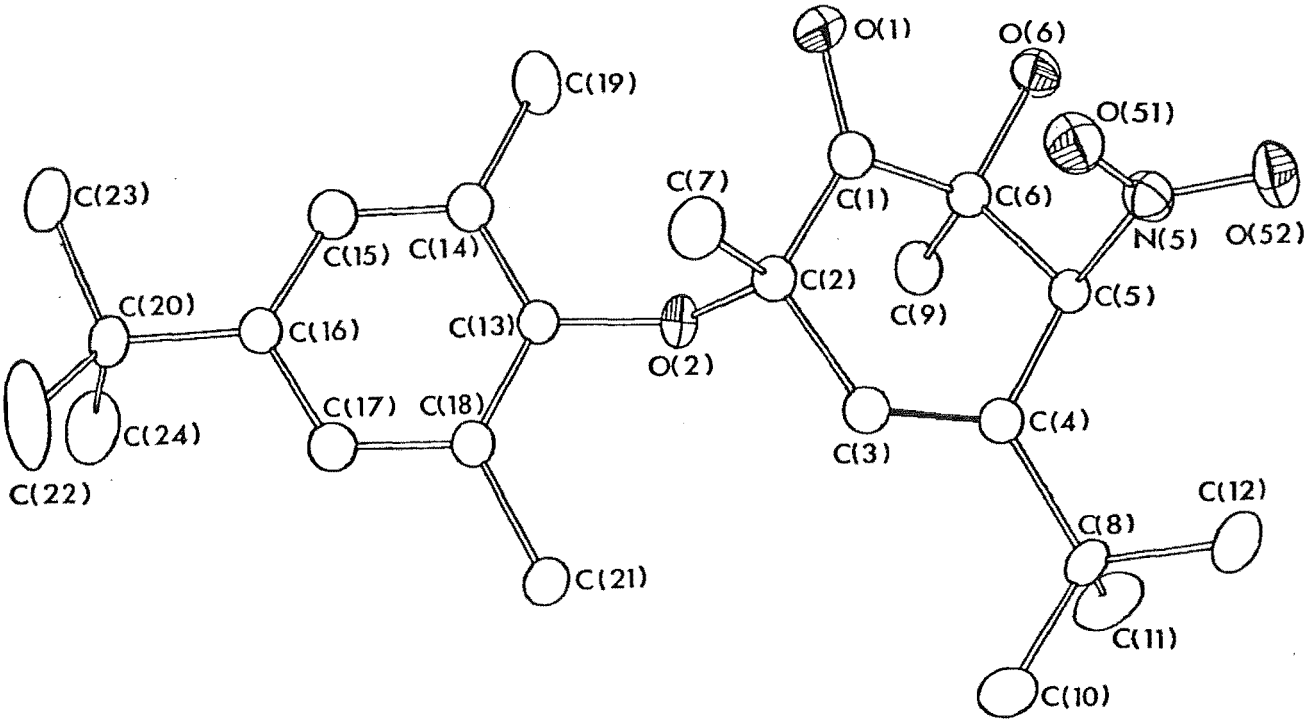
(77)



(109)



(74)



(109)

FIGURE 20.

ACKNOWLEDGEMENTS

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Last, but by no means least, I would like to extend a special word of thanks to my family without whose support this thesis would not have been possible.